



# AMERICAN JOURNAL

## OF

# OBSTETRICS AND GYNECOLOGY

### ADVISORY EDITORIAL BOARD

FRED L. ADAIR  
BROOK E. ANSFACH  
WILLIAM T. BLACK  
LUCIES E. BURCH  
WALTER W. CHIPMAN  
WILLARD R. COOKE  
HARRY S. CROSSEN  
THOMAS S. CULLEN  
ARTHUR H. CURTIS  
CARL H. DAVIS  
WILLIAM C. DANNOTH  
WALTER T. DANNEBRIER  
JOSEPH B. DELEE  
ROBERT L. DICKINSON

PALMER FINDLEY  
C. FREDERIC FLUHMANN  
ROBERT T. FRANK  
JOHN R. FRASER  
GEORGE GELMHORN  
WILLIAM P. HEALY  
F. C. IRVING  
FLOYD E. KEENE  
JENNINGS C. LITZENBERG  
FRANK W. LYNCH  
JAMES C. MASSON  
JAMES R. MCCORD  
C. JEIT MILLER  
NORMAN F. MILLER  
CHARLES C. NORRIS

EMIL NOVAK  
EVERETT D. PLASS  
ISIDOR C. RUBIN  
JOHN A. SAMPSON  
OTTO H. SCHWARZ  
H. J. STANDER  
FRED J. TAUSSIG  
HOWARD C. TAYLOR, JR.  
PAUL TITUS  
GEORGE GRAY WARD  
RAYMOND E. WATKINS  
BENJAMIN P. WATSON  
KARL M. WILSON

### OFFICIAL ORGAN

THE AMERICAN GYNECOLOGICAL SOCIETY; THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS, AND ABDOMINAL SURGEONS; NEW YORK OBSTETRICAL SOCIETY; OBSTETRICAL SOCIETY OF PHILADELPHIA; BROOKLYN GYNECOLOGICAL SOCIETY; ST. LOUIS GYNECOLOGICAL SOCIETY; NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY; BALTIMORE OBSTETRICAL AND GYNECOLOGICAL SOCIETY; CHICAGO GYNECOLOGICAL SOCIETY; CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS; AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY; WASHINGTON GYNECOLOGICAL SOCIETY

---

### EDITORS

GEORGE W. KOSMAK . . . . . HUGO EHRENFEST

---

VOLUME 30

JULY—DECEMBER, 1935

---

ST. LOUIS

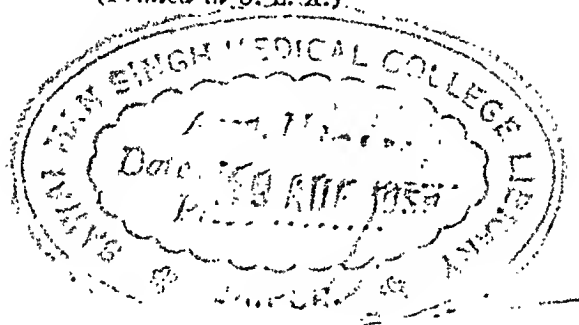
THE C. V. MOSBY COMPANY

1935



COPYRIGHT 1935, BY THE C. V. MOSBY COMPANY  
(All Rights Reserved)

(Printed in U. S. A.)



Press of,  
The C. V. Mosby Company  
St. Louis

# American Journal of Obstetrics and Gynecology

---

VOL. 30

ST. LOUIS, JULY, 1935

NO. 1

---

## Original Communications

---

### THE RÔLE OF BLOOD TRANSFUSION IN THE TREATMENT OF OBSTETRIC HEMORRHAGE\*

WILLIAM J. DIECKMANN, B.S., M.D., AND EDWIN F. DARBY, M.D.,  
CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, the University of Chicago, and  
the Chicago Lying-in Hospital)*

MORTALITY statistics indicate that over 10 per cent of the maternal deaths are due to puerperal hemorrhage, an inclusive term for postpartum hemorrhage, placenta previa, and abruptio placentae. The figure is increased to at least 28 per cent if deaths due to hemorrhage from ectopic pregnancy, abortion, and the accidents of labor (lacerations or rupture of the vagina, cervix, or uterus) are included. The maternal mortality rate in the United States for these various conditions is essentially the same for the years of 1910, 1920, 1926, 1927, and 1928. During a recent four-year period, 246, or 26 per cent, of the maternal death certificates in Chicago have given hemorrhage, placenta previa, abruptio placentae, or ectopic pregnancy as the primary cause of death. Similar figures have been published recently for Philadelphia.

A report of maternal mortality in fifteen states, recently published by Children's Bureau of U. S. Department of Labor, indicates that 11 per cent of the deaths were due to puerperal hemorrhage. Hemorrhage was the direct cause of death in 347 patients with placenta previa, in 374 patients with postpartum hemorrhage, and in 70 patients with abruptio placentae and other similar causes. The committee noted

---

\*Read before the Chicago Gynecological Society, December 21, 1934.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

that patients with placenta previa were subjected to operative procedures without coincident blood transfusion, although great losses of blood had occurred. They also stated that "transfusion would doubtless have been given more frequently if equipment for blood typing and for giving transfusion had been at hand." They recommended that *all physicians practicing obstetrics give particular consideration to the value of blood transfusion.*

Since May 28, 1931, there have been 22 maternal deaths at the Chicago Lying-in Hospital and 6, or 27 per cent, of these were due to hemorrhage. Three of these patients died from rupture of the uterus, with hemorrhage as a contributory factor. It is evident from these figures that obstetric hemorrhage is of grave import, and despite our voluminous, and occasionally enthusiastic, reports of the treatment of these various conditions, the mortality has not decreased in the past twenty years. What is the explanation for this appalling mortality?

The use of transfusion with a known compatible blood has been possible only since 1910. Why has the modern obstetrician failed to lower the mortality due to obstetric hemorrhage despite the earlier teachings of Blundell and Hicks as to the value of blood transfusion? The answer to this question is that either an insufficient amount of blood is given or too great an interval of time elapses between the hemorrhage and transfusion, with resultant irreparable damage to the vessel walls, brain, and other vital structures because of the anoxemia. If the immediate or primary cause of death in these patients is lack of blood, then the patient should survive when the blood loss is replaced by transfusion.

The physician must have a fair knowledge of such phenomena as water balance, fluid exchange between the vascular system and the tissue spaces, blood and plasma volume, the optimum concentration of hemoglobin, serum protein and fibrinogen, blood pressure and shock, before he can properly treat obstetric hemorrhage. These various important constituents of the blood and physicochemical phenomena are mentioned only briefly, if at all, in the medical curricula. This knowledge is acquired subsequently from practice and usually costs the lives of the patients.

Most obstetric textbooks state that the pregnant woman at term is plethoric and has an increased volume of blood, and that because of this fact a blood loss of 500, 1,000, or even 2,000 c.c. is not of great significance.

Dieckmann and Wegner determined the blood volume, hemoglobin, and many other constituents of the plasma on the *same women* throughout pregnancy. They found that the pregnant woman did not have an increased blood volume, enabling her to withstand a blood loss of 1,500 to 2,500 c.c., as described by Williams, DeLee, and others. The average increase in blood volume was 23 per cent, but due to the patient's gain in weight, there was no increase in the amount of blood per kilo-

gram. Furthermore, after delivery no increase in the amount of blood per kilogram or in the concentration of the hemoglobin was noted. In normal pregnancy it was found that there was a small but definite decrease in the hemoglobin concentration, but an increase in the total amount.

It is difficult to select any constituent of the blood as an important index of blood loss, but a deficiency in hemoglobin content probably manifests itself earlier than any of the others. Therefore, the determination of the hemoglobin should be a part of the prenatal care. Undue emphasis is placed on the erythrocyte count and not enough on the hemoglobin. The erythrocytes should be regarded merely as a taxicab for the hemoglobin, and emphasis should be placed on the

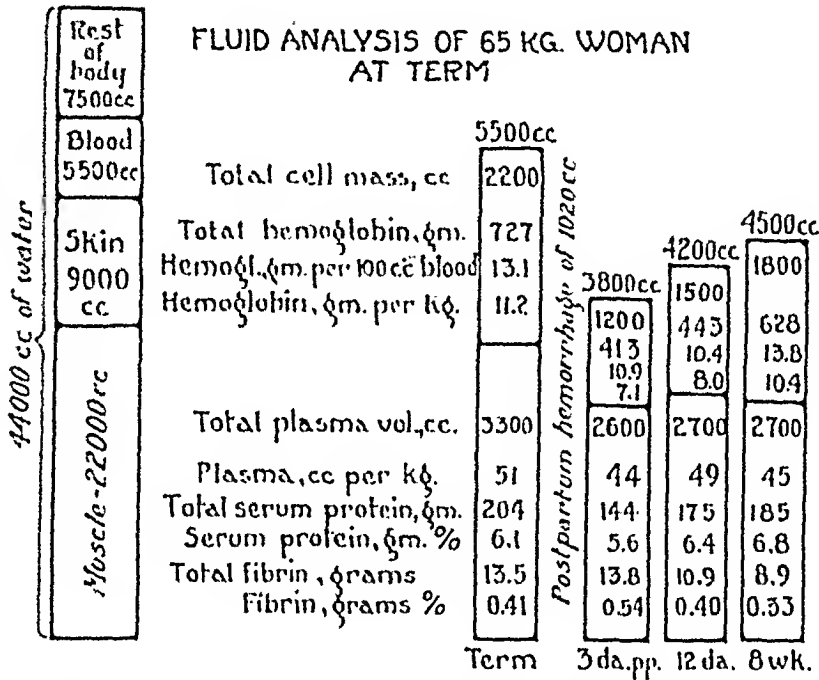


Fig. 1.—Water content of a patient at term weighing 65 kg., and the blood and plasma volumes, hemoglobin and other constituents of the blood during the antepartum and postpartum periods.

determination of the hemoglobin content rather than on the number of erythrocytes. Several investigators have found that the normal hemoglobin for women ranges from 12 to 16 gm., with an average of 14.3 gm. of hemoglobin per 100 c.c. of blood, per 5,000,000 erythrocytes, per hematocrit of 43 per cent. Dieckmann and Wegner found the average hemoglobin in normal pregnant women at term to be 12.4 gm. per 100 c.c. of blood. The hematocrit reading, which is a far more accurate method than the hemocytometer for determining the amount of erythrocytes, was 38.1 per cent.

The hemoglobin determination is part of the routine prenatal examination in most hospitals, but it is just within the past few years

that the work of Kerwin, Moore, Galloway, Bland, and others has indicated the importance of routine determinations. In 1931, Adair made it a rule of the Chicago Lying-in Hospital that every patient must have a hemoglobin determination. During a six-month period, 23 per cent of the prenatal patients had a hemoglobin content under 10 gm.

The water content of a patient at term weighing 65 kg. is shown in Fig. 1. It is apparent from the graph that the blood volume forms only a small part of the total fluid. If the amount of water is increased at one point, it is soon carried away by the blood and either distributed evenly throughout the body tissues or excreted by the kidneys, lungs, bowels, or skin. The blood and plasma volumes, hemoglobin and other constituents of the blood during the antepartum and postpartum periods are also shown in Fig. 1. It is notable that a measured blood loss of 1,020 c.c. produces marked changes in the blood and plasma volume and in the concentration and total amount of hemoglobin, hematocrit, serum protein, fibrinogen, etc. This patient was not transfused because of the study but was watched very closely. A relatively rapid increase of the plasma volume, serum protein, and fibrin, but a slow return of the hemoglobin and blood volume to normal may be noted.

The immediate effect of loss of blood from the vascular system is a parallel decrease of all of the constituents of the blood, thus producing no change in the relationship of hemoglobin to cell count or cell volume. The blood volume is a constant for the individual and if a reduction occurs, a compensatory increase in the plasma volume takes place and persists until new hemoglobin has been produced. The plasma is increased by the passage of fluid and some serum protein from the tissue spaces into the blood stream. Adolph and coworkers state that after a hemorrhage in dogs the mean rate of plasma dilution per minute amounts initially to about 0.25 c.c. per kilogram. These phenomena are demonstrated by the data given in Fig. 1 and Table I.

Table I (Keith, 1917) also demonstrates the rapid increase of the plasma volume but a slower return of hemoglobin and blood volume. This patient was a soldier with a simple comminuted fracture of the left femur. A large hematoma of the left thigh developed, with no external bleeding.

TABLE I. M. M.\*

DAY	BLOOD VOLUME		PLASMA VOLUME		HEMO- GLOBIN	HEMATOCRIT
	TOTAL C.C.	C.C. PER KG.	TOTAL C.C.	C.C. PER KG.		
1	4000	64	2525	69	83	37
2	4420	71	3025	83	74	31
4	4560	77	3375	96	63	26
7	4760	80	3710	106		22
12	5400	89	3730	105	68	31
16				.	81	33
22	5550	96	3440	100	97	38

\*Taken from Keith, 1917.

A syndrome, generally known as "shock," frequently occurs after hemorrhages or difficult deliveries, especially when attended by hemorrhage. When the various conditions which may cause shock are analyzed, the reduction of the blood pressure and of the circulating blood volume is common to all. Either one of these may be the primary change, the other secondary. Absolute loss of blood volume is the primary change in hemorrhage. The blood volume is also decreased in shock not due to hemorrhage from the vascular system. Obviously, the phenomena of shock and hemorrhage are similar.

Blalock states that because of the decrease in blood volume incidental to the hemorrhage, a compensatory vasoconstriction maintains the arterial blood pressure at or near the normal level. If the blood volume continues to diminish, the blood pressure decreases even though vasoconstriction is maintained. If the blood pressure remains depressed for a considerable length of time, the vasoconstriction mechanism fails and vasodilatation results. He also states that transfusion is of no avail in animals with vasodilatation. Blalock concludes that "an increase in the concentration of the blood, a negative response to transfusion, and marked alteration in the tissues of the body can be produced by hemorrhage."

Keith and Cannon, on the basis of clinical observation and the degree of blood volume reduction, have grouped patients in shock into compensated, partially compensated and uncompensated. The salient findings in the latter group, which is the most serious, are as follows:

If the hemorrhage equals or exceeds one-third of the blood volume, certain new factors are introduced which prevent the reformation of the blood volume by an increase in the plasma. These new factors have to do primarily with the sudden diminution in blood volume rather than a hemoglobin deficiency, because by repeated small hemorrhages the hemoglobin may be decreased to 20 per cent of the normal without any untoward symptoms. A massive hemorrhage results in a sudden and marked drop in blood pressure, inefficient circulation and stagnation of the blood in the capillaries. These patients are dangerously ill. They are restless, very thirsty, vomit frequently, and their extremities are very cold. The pulse is imperceptible and the systolic blood pressure may be decreased to 60 mm. Hg or less. The heart rate on auscultation ranges from 120 to 180. A heart rate below 100 occasionally occurs in this type of patient and is almost invariably fatal. The blood volume is below 65 per cent.

Because of the inefficient circulation, anoxemia results and changes occur in the vessel walls which permit not only fluids but also plasma protein to pass out. Thus a vicious circle is produced, i.e., the hemorrhage causes a decrease in blood volume which results in shock, which, in turn, causes a further reduction in blood volume, and so on. If hemoglobin or erythrocyte determinations are made on cutaneous blood, the results are usually much higher than if made on venous blood because of the capillary stagnation. Thus, despite the hemorrhage, the paradoxical situation of a rapidly increasing hemoglobin,

cell volume and cell count of either cutaneous or venous blood, especially the former, arises and indicates progressively increasing shock and a poor prognosis.

Significant relationships between the systolic or diastolic blood pressure and pulse rate have been reported by various investigators, but it must be emphasized that no rule holds true for all cases. The pulse pressure is approximately one-half of the diastolic and one-third of the systolic pressure. It should always be 30 mm. Hg or more. McKesson states that if it is 20 mm. or less for more than twenty minutes, the patient either dies at once or within three days (because of pathologic changes in the brain cells produced by the cerebral anemia). A systolic blood pressure of 80 or less is of serious import.

Archibald and McLean state that of 17 soldiers with the systolic pressure below 75, only three rallied, and they also died later. They conclude that the diastolic pressure is the most important, and that it must be raised by treatment if recovery is expected. Phenister and coworkers conclude that "in states of circulatory depression, the blood pressure is an inadequate index of the seriousness of the condition." They state further that if an operation is performed on an animal which has its blood volume reduced by hemorrhage or trauma, a further minimal hemorrhage might result in death. In patients with hypertension, the systolic and diastolic pressures may drop 50 to 150 mm. within a few minutes, and even though they may still be within the normal limits, the patient will present all the features of severe shock because the pressure is abnormally reduced for that individual.

It is evident that hemorrhage has many physiologic effects, which Adolph and coworkers summarize as follows:

The primary effects of loss of blood from circulation are to decrease the rate of blood flow and oxygen flow to most tissues. To this situation the circulation responds by increase in heart rate, discharge of adrenalin, discharge of blood from the spleen, local vasoconstrictions, and local persisting ischemias. The respiration responds to the local asphyxia in its centers and to the pouring of lactate into the circulation by hyperventilation, followed eventually by asphyxia and cessation of breathing. In the capillaries, fluid flows into the blood from tissue spaces, water excretion by the kidneys is diminished, and various dissolved constituents interexchange in response to the lowered pressures, to the anoxia, and to the altered types of tissue metabolism.

The potential indication for blood transfusion in a patient with an obstetric hemorrhage is a hemoglobin which we have arbitrarily set at less than 10 gm. per 100 c.c. of blood. Obviously, a hemoglobin estimation immediately after a hemorrhage is of little value. It may even be increased due to shock. The ideal criterion would, therefore, be the blood volume, but since its determination is impractical, the best guide is the patient's clinical condition and the blood loss. We have been making accurate determinations of the hemoglobin loss at delivery and cesarean section. The average blood loss in a low cervical cesarean section is 539 c.c., with a range of from 100 to 1,430 c.c. Our rule is to estimate the blood loss and multiply it by two or by three,

if the patient's hematocrit is 30 per cent or less. The patient should be transfused if the blood loss can be determined with a reasonable degree of accuracy and amounts to 20 per cent or more of the blood volume, providing that her hemoglobin was more than 10 gm. at the onset. Transfusion is imperative if the hemoglobin was less.

Many patients who have been bleeding for several days may enter the hospital apparently in good condition, but before any manipulation or examination is carried out which might cause further bleeding, a transfusion should be given. The reason for this is that with a slow hemorrhage the hemoglobin can be decreased to as low as 2.8 gm., or 20 per cent of the normal. These patients are quite likely to die if any additional blood is lost. A sudden blood loss entailing 40 to 50 per cent of the hemoglobin usually ends fatally.

There is a slight hemoconcentration in normal pregnant women during labor. The hemoglobin and other constituents may increase 25 per cent in toxemic patients as a result of the concentration. Anesthesia intensifies these phenomena. Therefore, the blood lost at delivery may, and often does, contain a greater concentration of hemoglobin than would be expected from a determination of hemoglobin which had been made during pregnancy or early in labor.

Attention must be given to the patient's weight in correlating blood loss with clinical conditions. It is obvious that a blood loss of 1,000 c.c. from a patient weighing 50 kg. and having a blood volume of 4,000 c.c. is of more serious import than the same amount from a woman weighing 70 kg., with a blood volume of 5,600 c.c. A large amount of serum protein and fibrin is lost in addition to the hemoglobin if the hemorrhage is severe. A certain concentration of these substances is essential for the proper functioning of various organs and the exchange of water in the tissues.

Five to ten days are required for the return of the serum protein to normal. Fibrinogen, one of the components necessary for blood coagulation, requires one or two days for regeneration. If the patient has had a marked hemorrhage and is given sufficient fluid for the blood volume to return to normal, it occasionally happens that the fibrinogen concentration is so low that proper coagulation does not occur, thus permitting the bleeding to continue. A low concentration of fibrinogen may be a factor in the continued hemorrhage or oozing observed in certain cases of abruptio placentae and postpartum hemorrhage.

Transfused blood, as far as we are able to determine, functions just as well as the patient's own blood. The longevity of the erythrocyte in man ranges from eighteen to one hundred days, with an average of thirty days. The transfused erythrocyte, both in vitro and in vivo, functions normally, and its life is apparently not shortened. Serum protein, fibrinogen, and platelets also function in a normal manner in



the new host. If the plasma protein concentration is increased above the normal for that individual as a result of the transfusion, the excess amount disappears from the blood stream within seventy-two hours.

The hemoglobin concentration on the day following a transfusion is occasionally lower than it was before. Krogh and others have demonstrated that only 40 to 50 per cent of the capillaries are normally open at any time, and still fewer are open in patients with a decreased blood volume. Furthermore, with a deficient blood volume there would be a decreased bore of the arterioles because of the vasoconstriction. Following the transfusion, the arterioles dilate and more capillaries open up; thus, although the total amount of hemoglobin is increased, the concentration is decreased.

A summary of our transfusions and data from selected cases will illustrate the results and methods of treatment. From May 28, 1931, to Sept. 30, 1934, there have been 8,998 deliveries at the Chicago Lying-in Hospital, in which more than 274 transfusions have been given. Because of technical difficulties in the Record Room, we were unable to have access to all of the blood transfusion charts, but believe that we have at least 90 per cent of them. From June 1, 1928, to May 27, 1931, at the old Chicago Lying-in Hospital, in 8,672 deliveries, only 22 patients received transfusions. The average amount of blood transfused was 403 c.c. A comparison of data is difficult. The blood loss of the patients in our series may have been greater than those in the old hospital, or their blood volume may have been lower, or we are better prepared to transfuse. The ability to transfuse rapidly, repeatedly, and safely is sufficient reason for the large number of trans-

TABLE II. TRANSFUSIONS AT THE CHICAGO LYING-IN HOSPITAL

CONDITION	NUMBER OF		AVERAGE AMOUNT OF BLOOD PER	
	PATIENTS	TRANSFUSIONS	PATIENT	TRANSFUSION
<i>Obstetric Cases</i>				
			C.C.	C.C.
Postpartum hemorrhage	33	41	748	602
Placenta previa	22	29	824	670
Abruptio placentae	13	25	1183	615
Operative hemorrhage	14	25	1035	660
Abortion	10	12	685	570
Chorionepithelioma	1	11 (6 wk.)	7000	636
Anemia of pregnancy	21	39	1054	568
Infection, ectopic pregnancy, etc.	18	32	909	525
Total	132	214	919	608
<i>Gynecologic Cases</i>				
Uterine myomas	16	28	1026	588
Menorrhagia	10	11	635	577
Carcinoma of uterus	5	9	1010	561
Infections, shock and post-operative hemorrhage	11	14	755	582
Total	42	62		

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.

DIECKMANN-DAILY: BLOOD TRANSFUSION IN OBSTETRIC HEMORRHAGE 9

fusions. The routine hemoglobin determination enabled us to detect a severe grade of anemia in 21 patients who were given 39 transfusions. The total maternal mortality is slightly less in the new than in the old hospital, and there have been no fatalities in the new hospital, either immediate or remote, due to blood transfusion.

The data for the transfusions given are listed in Table II, which illustrates the value of large and repeated transfusions, particularly the amount of blood given to each patient for the various conditions. Thus the average amount of blood per transfusion is 608 c.c., and the average per patient is 919 c.c.

Most normal adults can tolerate a blood loss of 500 c.c. Therefore, 600 to 800 c.c. of blood should be the amount of the transfusion in patients with evidences of hemorrhage. The transfusion may have to be repeated one or more times if the hemorrhage has been massive.

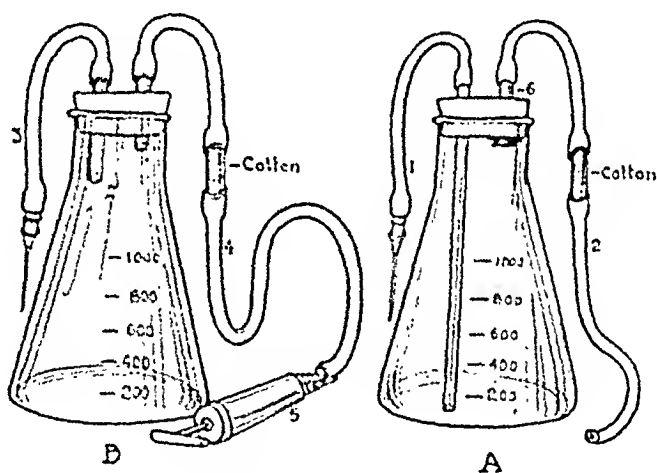


Fig. 2.—Flasks equipped for taking the blood.

Our technic of the treatment of severe anemia, whether due to acute or chronic blood loss from obstetric hemorrhage or blood dyscrasia, is described in the case reports.

#### METHOD

The method for citrate blood transfusion is as follows: 50 c.c. of a 4 per cent solution of sodium citrate (U.S.P. VIII—this number is very important) are used for amounts of blood ranging from 400 to 700 c.c. Although this amount of citrate will inhibit clotting in 1,000 c.c. of blood, if more blood than 700 c.c. is to be withdrawn, another 10 c.c. of citrate solution are added. In a case of purpura hemorrhagica in which bleeding continued from an operative incision, despite citrate transfusion, whole blood was transfused by the multiple syringe method.

The transfusion set consists of the bottle, rubber tubing, needles, syringes, and citrate solution, all of which have been properly wrapped together and autoclaved. The bottle for taking the blood is equipped as in Fig. 2, A. It is placed in a pan of water at 41° C.; the top of the bottle must be below the level of the arm. The suction tube (1) for the donor is 10 inches long and of one-eighth inch bore. The

citrate solution, using mouth suction, is drawn into the bottle and then a 15 or 16 gauge needle is inserted into one of the arm veins, pointing away from the heart. The flask is given a rotary shake with every 100 c.c. of blood. Usually 700 c.c. of blood can be aspirated in five to ten minutes. The flask is then fitted as in Fig. 3, *C*, the rubber tubing (*8*) which is 6 feet long and of five-thirty-seconds inch bore is immersed in a pan of water at 40 to 42° C., and a 17 or 18 gauge needle inserted into the recipient's arm, pointing toward the heart. The first 50 to 100 c.c. are injected over a period of three to five minutes, and if the patient complains of tingling, body pains, precordial oppression, or extreme anxiety the rate of injection is slowed. If the patient complains of pain in the lumbar region or tightness in the chest, or if cyanosis, dyspnea, edema, a slow thready pulse, chill, fever, delirium, or convulsions are noted the transfusion must be stopped at once, and the typing and matching rechecked. A drop of alcohol in the long glass suction tube (*7*) indicates whether or not the blood is running. In children and in patients with collapsed veins, the

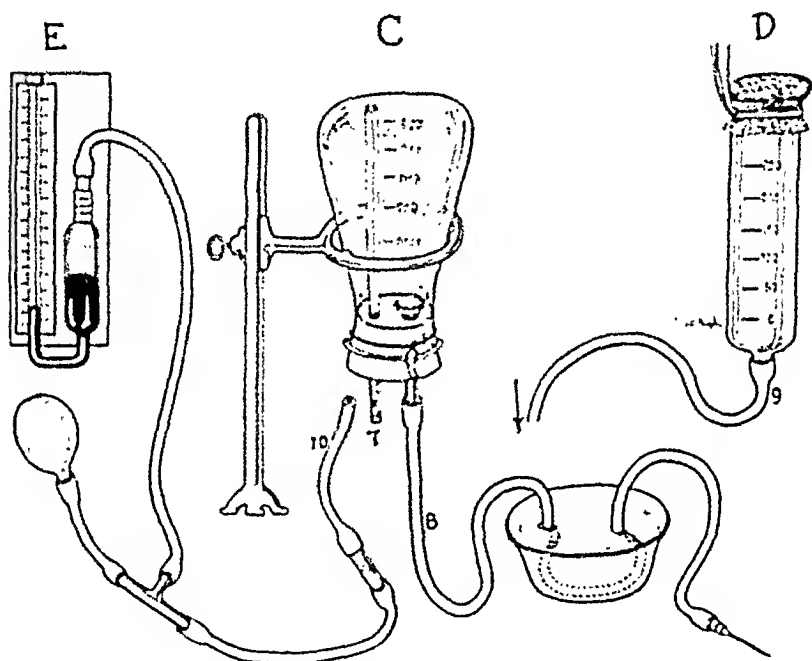


Fig. 3.—Set-up for giving the transfusion.

blood pressure manometer (*E*) may be connected (10 to 7) with the transfusion bottle and 150 to 200 mm. of mercury pressure used to force the blood in. The blood can also be removed from the bottle and poured into a salvarsan flask (*D*). In cases of severe hemorrhage and shock in which intravenous glucose or saline solution and repeated blood transfusions are necessary over a period of hours, the blood may be poured into the salvarsan flask. If this latter procedure is to be used, the set-up illustrated in Fig. 2, *B* will be found more convenient for obtaining the blood. Suction can be made with the mouth or a pump (*5*). The transfusions can be performed in the operating room or in the patient's home. No other set-up than that described is necessary.

#### CASE REPORTS

CASE 1.—Abruptio placentae (Table III). The patient was delivered by cesarean section. A stillborn fetus was removed, with a blood clot measuring 700 c.c., which represents at least 2,000 c.c. of blood. The uterus contracted well and the hemorrhage at time of operation was minimal; the patient was in shock. Subsequently,

TABLE III. ABRUPTIO PLOENTAE

TIME	TEMPERATURE	PULSE	BLOOD PRESSURE	REMARKS	TREATMENT			DATE	BLOOD DETERMINATIONS			
					20% GLUCOSE INTRAV. C.C.	BLOOD TRANS- FUSION C.C.	RINGER'S SOL. HYPODER- MOCLYSIS C.C.		HEMO- GLOBIN GM. %	HEMA- TOCRIT %	SERUM PROTEIN %	FIBRIN %
9/3/33: 3:00 A.M.				Sudden abdominal pain. Vaginal hemorrhage of 200 c.c.				9/3/33	6.8	22.5		0.161
4:30 A.M.	36.4	112		Patient pale and ill. Uterus hard. No F.H.T.				9/4/33	7.7	22.5	5.0	0.440
5:45 A.M.		120	100/7	Exsanguinated. Uterus large, tender, and does not relax				10/2/33	10.6	36.0	8.7	
6:40 A.M.			108/7	Cesarean section	800	800		11/9/33	13.0	43.0		
7:30 A.M.				Air hunger, shock			2000					
11:00 A.M.		86	130/85		500	600						
1:20 P.M.				Persistent hemorrhage, subtotal hysterectomy	200	900	1000					
6:30 P.M.	37.0	84	145/85									
9/4/33: 6:00 A.M.	38.2	96		Fluid intake 9350 c.c. 24-hour output 1250 c.c.								

TABLE IV

TIME	BLOOD PRESSURE	PARENTERAL FLUID	REMARKS	HEMOGLOBIN GM. PER 100 C.C.	HEMA-TOCRIT %	SERUM PROTEIN GM. %
12:30 A.M.			Patient delivered			
First day 4:45			Admitted to hospital in shock, ex- tremities cold, no radial pulse. In- fundin M III intravenously.	6.9	23	
5:15		1000 c.c. 20% glucose over 90 min. 2000 c.c. Ringer's sol. by hypo- dermoeclysis		6.2	22	3.9
5:30	74/40					
6:15	50/7		Patient awake. Placenta expressed by modified Crede method.			
6:30	70/46		Adrenalin 0.5 c.c. intramuscularly			
6:45	74/40	500 c.c. 6% aescia sol.				
7:30	72/42	700 c.c. blood				
9:10		500 c.c. 5% glucose	Uterus packed			
9:45	75/50	500 c.c. 6% aescia sol.	Adrenalin M III intravenously. Ephedrine 0.03 subcutaneously			
10:45	82/50	850 c.c. blood				
11:15	100/62	1000 c.c. 5% glucose				
1:30 P.M.	110/70		12-hour intake 12,000 c.c. Output 4,300 c.c.	7.5	23	3.4
Second day			24-hour intake 13,000 c.c. Output 5,000 c.c.	7.5	24	4.0
Third day		750 c.c. blood		6.9	21	4.1
Fourth day				8.4	27	4.7
Eighth day				9.2	28	5.5
Nineteenth day				9.9	30	6.2

she began to bleed and a subtotal hysterectomy was performed five hours later. Note: (1) the large amount of blood which was given in twelve hours without any change in hemoglobin or hematocrit; (2) the large fluid intake with a comparatively small output; (3) the very low fibrin content (normal 0.3 to 0.5) which was a probable factor in the constant oozing; (4) the low serum protein due to the restoration of the plasma volume to normal, but the inability of the body to maintain a normal concentration of proteins because of the excessive loss by hemorrhage.

CASE 2.—Intrapartum and postpartum hemorrhage (Table IV). This patient was delivered at home by a private physician. Note (1) the primary treatment for shock and hemorrhage; (2) the tremendous fluid intake required to maintain the blood pressure; (3) the hemoglobin only increased from 6.2 to 8.4 gm. per 100 c.c. despite the transfusion of 2,300 c.c. of blood in forty-eight hours; (4) the abnormally low serum protein due to the excessive hemorrhage and resultant plasma dilution; (5) the more rapid return of the serum protein to normal.

CASE 3.—Spontaneous rupture of the uterus. The patient was in labor and at term. The rupture occurred at 11:35 P.M. There was no palpable radial pulse or audible blood pressure. Between 11:50 P.M. and 12:45 P.M. the fetus and uterus were removed; she was given two transfusions each of 500 c.c. of blood, 1,200 c.c. of 20 per cent glucose solution intravenously, and 700 c.c. of saline solution by hypodermoclysis. Seven hours later the pulse was 140, the blood pressure 90/70, and respirations 36. She received another transfusion of 600 c.c. of blood and 700 c.c. of glucose solution intravenously. The hemoglobin was 10.6 nine days before labor, and thirty-six hours after labor, despite the transfusion of 1,600 c.c. of blood, it was 8.8 gm. Recovery was uneventful.

CASE 4.—Severe anemia of pregnancy (Table V). The patient did not have a hemorrhage from any source. She was given 4,600 c.c. of blood during a period of twenty-four days. A normal infant was delivered at term and up to the present time the anemia has not recurred. Note (1) the relatively constant plasma volume, but the marked increase in the cell mass; (2) the hemoglobin per kilogram was ex-

TABLE V. SEVERE ANEMIA OF PREGNANCY

L. H. #54736

DATE	HEMO- GLOBIN GM. 100 C.C.	HEMATO- CRIT %	ERYTHRO- CYTES MILLIONS	HEMO- GLOBIN GM. KG.	BLOOD VOLUME C.C.	PLASMA VOLUME C.C.	BLOOD TRANS- FUSION C.C.
1932							
2/10	8.1		2.64				
4/18	6.4		1.70				
4/27	5.1	16	1.75	3.3	3910	3290	600
5/ 5	6.2	20	2.24				600
5/ 9	7.2	23					700
5/13		32					700
5/16	8.8		2.58				700
5/20	11.0		2.90				600
5/26							700
6/ 7	11.5 (delivery)	33	3.64	9.0	4780	3200	
7/19	11.6	37		9.1	4140	2610	
10/18	11.7	35	4.50	10.5	4620	3000	
12/ 5	13.4	39	3.33	14.7	5640	3440	
10/23/33	12.2	39	3.70				
11/19/34	10.5	36	3.93				

tremely low, and indicates the marked anemia better than the hemoglobin concentration; (3) the hemoglobin per kilogram did not reach normal limits until after the seventh transfusion.

CASE 5.—Pregnancy complicated by severe purpura hemorrhagica (Table VI). Note that large transfusions increased the hemoglobin, platelets and serum protein to a low normal despite a massive postpartum hemorrhage.

TABLE VI. SEVERE ANEMIA OF PREGNANCY DUE TO BLOOD DYSCRASIA

M. S.

TIME	HEMO- GLOBIN GM. 100 C.C.	HEMATO- CRIT %	SERUM PROTEIN GM. %	PLATELETS	ERYTHRO- CYTES MILLIONS	BLOOD TRANS- FUSION C.C.
First day	3.5	10	5.0	22,000	0.95	
Second day	3.5	10		19,000	1.69	800
Third day	6.7	18	5.6	28,000	1.98	600
Third day	(Delivery, postpartum hemorrhage 1000+ c.c.)					
Third day	7.5	22			2.40	800
Fourth day	8.6	26	4.7	40,000	2.66	600
Fifth day	9.5	30	5.0	51,000	3.41	800
Twelfth day	10.8	33	6.0	116,000	3.60	
						Total 3600 c.c.

## COMMENTS

After a severe hemorrhage, while a donor is being obtained, the body must be kept warm by the application of external heat (electric baker). Saline or Ringer's solution should be given by hypodermoclysis, using 16 gauge needles. A 20 per cent solution of glucose may be injected intravenously. After 200 to 300 c.c. of glucose solution have been given, the rate of injection should be as slow as possible, yet maintaining the blood pressure. Five hundred cubic centimeters of 20 per cent glucose solution can be given intravenously in twenty to forty minutes without danger, but in patients who have had large hemorrhages, *more than this should never be given unless the patient is to receive 600 c.c. or more of blood.* Failure to observe this rule may result in the death of the patient. Twenty per cent glucose solution in amounts of 1,000 c.c. or more prolongs the coagulation time of the blood and because of its hypertonicity it draws large amounts of fluid into the circulation. This exhausts the reserve depots of fluid, and if further hemorrhage occurs there can be no increase in plasma volume.

The citrate method of transfusion is the only one suitable in obstetrics because of the necessity of speed. The methods used by us are modifications of those described by Kolmer, Hartman, Lewisohn and others and have been instituted to save time. In an emergency transfusion, we insist that the blood must be in the recipient's circulation within thirty to forty minutes, depending on the time required to obtain a donor. Eight hundred cubic centimeters of blood have been

taken and injected into the recipient in eleven minutes, but the average time required is twenty to thirty minutes.

There are *two dangers* associated with blood transfusion: (1) The immediate danger of an incompatible blood, in which case the patient almost invariably dies if more than 200 c.c. are injected. (2) The delayed danger of a severe reaction, or no reaction, without question of incompatibility, but characterized by an oliguria or anuria.

In 276 transfusions, chills occurred in 20 patients, and nausea, vomiting, urticaria, or pain in the chest or lumbar region in 10. Three patients received incompatible blood, the amounts varying from 50 to 100 c.c. Fortunately, all of these patients were conscious and at the first complaint of pain in the chest or lumbar region, the injection was stopped, the matching rechecked, and the blood found to be incompatible. A hemoglobinuria and partial oliguria developed, but none of the patients died. Renal function tests before discharge from the hospital showed no evidence of impaired renal function. Large amounts of intravenous glucose were given to these patients to produce a diuresis. Two of the transfusions were given by one man who, it should be noted, was careful and conscientious.

Typing serums purchased from reliable firms should be checked periodically. In a two-year period we had some impossible results on two occasions, and the Type III serum was found to have deteriorated to such a degree that agglutinins could not be demonstrated. This can be avoided by checking the serums or by using the Brem method of blood typing, in which the fresh cells and serum of a known Group II or III are matched with the serum and cells of the unknown.

The donor's cells should be matched with the recipient's serum, in addition to the determination of the blood group. There must be no agglutination or clumping at the end of thirty minutes at room temperature. The slide, plate or test tube (macroscopic technic) must be agitated periodically in order that one may be certain that the cells can move freely. *A sufficient number of cells must be used so that agglutination can occur and, most important, be detected.* One of the authors (W. J. D.) uses either a microscopic or a macroscopic method for determining the type, but insists on a macroscopic matching\* of the donor's cells and the recipient's serum, and watches for agglutination and/or hemolysis.

Rouleaux formation occurs to such a degree in patients with puerperal infection, probably because of the high fibrinogen, that the donor is usually reported as incompatible. An experienced serologist can usually distinguish between agglutination and rouleaux formation. Aging of the serum for two or three days decreases its rouleaux-forming properties.

\*Three-tenths cubic centimeter of the recipient's serum, 0.3 c.c. of 1 per cent sodium citrate in saline and 3 drops of the donor's blood are placed in a test tube.



The value of proper control of all transfusions is exemplified by the following: On the Obstetric Service of Washington University, during a period of six years ending in 1929, 147 patients were given 302 transfusions. The senior author was in direct charge of all transfusions for the greater portion of this period. No patient received an incompatible blood, and no deaths occurred because of a reaction. One patient had a marked oliguria, but recovered. The average amount of the transfusion was 602 c.c., and the largest was 850 c.c. One patient was given 9 transfusions (by Dr. T. K. Brown), a total of 7,150 c.c. of blood in four weeks. Transfusions by the citrate method, in which the blood was dropped from a needle into a container containing the anticoagulant, without careful supervision of technique, were followed by reactions (chill or temperature elevation of 2° or more) in 45 per cent of the cases. With the new method as described in this paper, in which suction was used to obtain the blood in a closed container and under careful supervision, the number of reactions decreased to 14 per cent. In 32 transfusions for all types of disease in patients of various ages, one of the authors (W. J. D.) observed no reactions. Dr. T. K. Brown has been in charge of the transfusion service since 1927, and if both periods, comprising 12 years, are combined, 877 transfusions have been given without any deaths attributable to an incompatible blood.

We have always preferred Group IV (Moss) donors because their cells contain no agglutinogens and, therefore, they cannot be clumped. This is an additional safeguard because a mix-up may occur in the laboratory, irrespective of elaborate checkings. In fact, the best check is for the physician himself to match the patient's serum and donor's cells (both obtained by him at that time) just prior to the transfusion. It is noteworthy that Dr. George Ives of St. Louis has performed personally more than 2,500 transfusions and attributes his success to personal supervision of typing, matching, preparation of the citrate solution, and to a preference for the Group IV (Moss) donor.

The treatment of a patient who has received an incompatible blood is as follows: Adrenalin and ephedrine for the shock, and adequate amounts of hypertonic glucose solution given intravenously to maintain a urinary output of at least 30 c.c. per hour. If more than 200 c.c. of blood have been given, the patient should receive sodium bicarbonate in sufficient amounts to produce a urine which is alkaline to brom-cresol-purple. This will necessitate 24 to 40 gm. by mouth, or the intravenous injection of 300 to 500 c.c. of a 4 per cent solution, as needed. If the blood is compatible, but an oliguria or anuria has developed, only hypertonic glucose should be given in an amount and concentration necessary to produce a secretion of urine.

## CONCLUSIONS

1. Obstetric hemorrhage is responsible for more than 10 per cent of the maternal deaths. The mortality has not decreased in the last twenty years despite the use of blood transfusions. If the maternal deaths due to hemorrhage from abortion, accidents of labor, and ectopic pregnancy are included the rate is increased to 28 per cent.

2. Hemorrhage decreases the blood volume and if massive enough initiates shock, resulting in death of the patient unless prompt treatment is instituted.

3. Some of the important constituents lost as the result of hemorrhage are water, hemoglobin, serum protein, and fibrinogen. They can be replaced by blood transfusion and parenteral fluid, and will function, so far as is known, as well as the patient's own blood and fluid.

4. The blood loss during hemorrhage is usually underestimated. It should be correlated with the patient's hemoglobin and blood volume or weight.

5. The citrate method of blood transfusion is ideal in the practice of obstetrics.

6. The mortality rate from obstetric hemorrhage can be lowered only if sufficient blood is transfused to raise and maintain the hemoglobin to approximately 10 gm. per 100 c.c. of blood.

7. The transfusion must be adequate in amount and must be given within a short time after the hemorrhage. Further transfusions may be given within a period of hours or spread over several days, depending on the amount of blood required and the clinical condition of the patient.

We are indebted to Dr. T. K. Brown and Dr. George Ives of St. Louis, Mo., for permission to use some of their data, and also for their many suggestions which have improved the technic for citrate blood transfusion.

## REFERENCES

- Adolph, E., Gerbasi, M., and Leportc, M.*: Am. J. Physiol. 104: 502, 1933.  
*Archibald, E., and McLean, W.*: Am. J. Surg. 68: 280, 1917. *Blalock, D.*: Proc. Inst. Med. 9: 405, 1933. *Brown, T. K.*: Personal communication. *Cannon, W. B.*: Traumatic Shock, New York, 1923, D. Appleton and Co. Committee on Maternal Welfare: Maternal Mortality in Philadelphia, 1931-1933. Philadelphia County Medical Society, 1934. *Dieckmann, Wm. J., and Wegner, C.*: Arch. Int. Med. 53: 71, 188, 345, 353, 527, 540, 1934. *Dieckmann, Wm. J., and Daily, E.*: To be published. *Erlanger, J., and Gasser, H.*: Ann. Surg. 37: 389, 1919. *Ives, G.*: Personal communication. *Keith, N. M.*: Med. Res. Comm. Report, No. 27, H. M. Stat. Off., 1919. *Krogh, O.*: Anatomy and Physiology of the Capillaries, New Haven, 1929, Yale University Press. New York Academy of Medicine: Maternal Mortality in New York City, 1930-32, Oxford University Press, London, 1933. *Roome, N., Keith, W., and Phemister, D.*: Surg. Gynec. Obst. 56: 161, 1933. United States Dept. of Labor: Maternal Mortality in Fifteen States. United States Government Printing Office, Washington, 1934, Pub. No. 223.

# THE SURGICAL TREATMENT OF OVARIAN DYSFUNCTIONS\*

## A CLINICAL AND PATHOLOGICAL STUDY

M. R. ROBINSON, M.D., F.A.C.S., NEW YORK, N. Y.

THE surgical treatment of properly selected cases of ovarian dysfunction is based upon histopathologic studies and clinical observations which prove that if a dysfunction repeats itself too frequently and forcibly, or if it persists for too long a time, the initial imperceptible structural alterations will ultimately develop into definite and permanent organic entities. This concept of physiologic pathology is gaining ground in all branches of medicine and causes the dogma, that functional diseases have no organic basis, to be relegated to the scrap heap of obsolete theories. Structure and function are indissolubly linked to each other.

In studying ovarian dysfunctions pathologically and clinically for a number of years, I became convinced that patients suffering from so-called ovarian hyper- or hypofunction for a long period of time, will present on careful bimanual palpation an enlargement of either one or both ovaries. If such patients have already been treated with endocrine preparations for a considerable period and, in the cases of ovarian hyperfunction with excessive uterine bleeding, have been curetted on a number of occasions, without relief, then a unilateral or a bilateral partial ovarian resection is indicated.

The validity of this radical procedure must be proved further by the following tests: (a) Does it render the expected therapeutic results in a fairly large proportion of cases? (b) Does the pathology of the resected ovarian tissue bear a sufficient correlation to the dysfunction in question? (c) Do the therapeutic results correspond to our present knowledge of interglandular correlations and of the influence of the vegetative nervous system upon the generative organs?

The material selected for this study was subjected to this searching analysis, especially the pathologic and clinical phases, and to facilitate this inquiry I have followed the accepted didactic classification of ovarian dysfunctions into hyper- and hypofunctions. I am fully aware of the scientific pitfalls to which such an arbitrary classification is heir, but until we possess means and methods of evaluating with physiologic accuracy the degree of disturbance in the primary and in the secondary endocrines involved in each type of dysfunction, the prevailing classification must remain our guide.

\*Read before the Section on Gynecology and Obstetrics, N. Y. Academy of Medicine, December 18, 1934.

## OVARIAN HYPERFUNCTION

CASE 1.—(Beth Israel Hospital) Pathol. No. 20406 L. V., aged fifteen, came under my observation on Dec. 28, 1931, complaining of almost continuous bleeding for the past eight months.

Menses began at thirteen, irregular, occurring every seven to eight weeks, profuse in amount, and lasting from five to six days. The last period set in eight months ago, and has not ceased as yet.

During this period of metrorrhagia she was treated with endocrine preparations, oxytocics, and in June, 1931, was curetted; all without avail.

*Physical Examination.*—A normally developed girl. No external evidences of endocrine disorder. Her secondary sex characteristics were feminine, complexion light, skin soft and smooth. No hirsuties. Rectopelvic examination disclosed a right ovarian cyst, the size of a hen's egg. Uterus retroverted. Left adnexa not palpable.

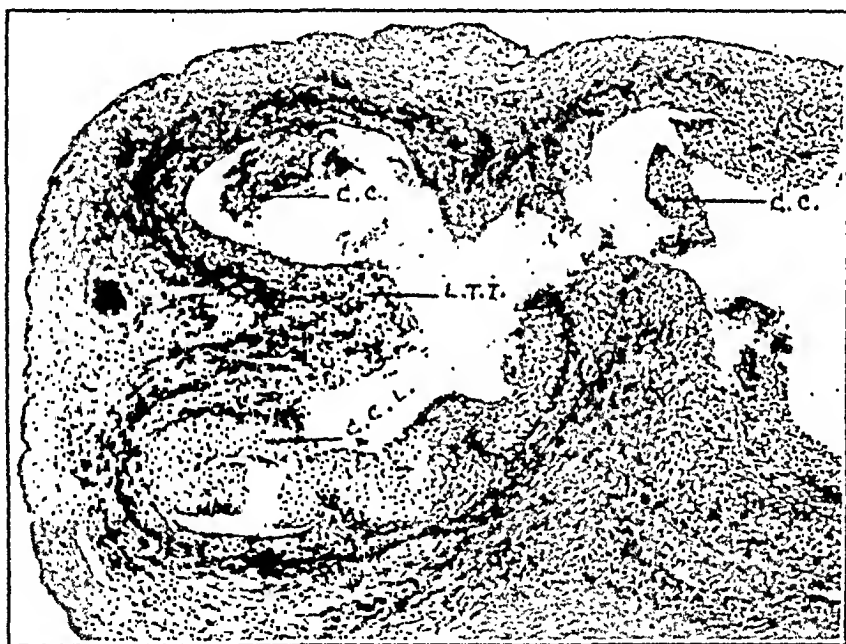


Fig. 1.—(Pathol. No. 20,406.) A persistent follicle cyst, often mistaken for a persistent corpus luteum cyst. Note the luteinization of the theca interna (L.T.I.), nonluteinized granulosa (G.C.), and a pseudoluteinization of granulosa (G.C.I.). (×200)

*Operation.*—On Jan. 5, 1932, curettage (for the second time). Because of the persistence of the bleeding I performed a laparotomy on Jan. 8, 1932, resected the cyst from the right ovary, removed the appendix, and corrected the uterine retroversion by a Baldy-Webster shortening of the round ligaments.

*Pathologic Findings.*—A glandular hyperplasia of the endometrium, with hyaline areas and leucocytic infiltration in the stroma. The ovarian stroma was edematous in parts, and contained many primordial follicles. The walls of the resected cyst were folded, and lined with a thick layer of luteinized theca interna, which in turn was covered with many layers of granulosa cells (Fig. 1). In some areas the granulosa cells had a luteinoid appearance.

*Postoperative Clinical Course.*—On the day following the resection of the persistent follicle cyst the uterine bleeding ceased. The first postoperative menstruation occurred two months later. Since March, 1932, up to the present she is free from metrorrhagia, and the menses occur every four to six weeks in normal amounts.

CASE 2.—Pathol. No. 21076 (Beth Israel Hospital). E. S., aged twenty-three, consulted me on May 10, 1932, because of persistent uterine bleeding for the past seven months, in varying amounts.

Menses began at fourteen: irregular, every five to six to seven weeks; painless, profuse, lasting about eight days. Her last normal period occurred before her last conception, twenty-one months ago. She was married two years; had given birth to a full-term normal child one year ago.

*Present Illness.*—Seven months ago she consulted a physician because of the persisting amenorrhea since her confinement, although she did not nurse her child. She received on three successive days, three hypodermic injections of anterior pituitary hormone, and began to bleed after the third injection. The bleeding continued irregularly for about thirteen days. The pituitary injections were resumed and in addition thyroid extract was given orally, for a period of three weeks. Five days after the cessation of this treatment the uterine bleeding returned and has continued



Fig. 2.—(Pathol. No. 21,076) Many atretic follicles (A.F.) in various stages of regression; some as hyalinized pinkish bodies of irregular shapes and dimensions, others with the central cavity not yet completely obliterated, in which some granulosa cells are still discernible. ( $\times 120$ )

almost uninterruptedly for the past six months. On March 29, 1932, she was curetted because of the persisting metrorrhagia, without avail.

*Examination.*—A well-developed female of light complexion weighing 224 pounds; has gained 70 pounds since her confinement. Primary and secondary sex characteristics normal. Basal metabolism normal. Blood: R.B.C. 3,980,000; leucocytes 34; monocytes 6; blood platelets 247,740; bleeding time three minutes; coagulation time 4.5 minutes. Vaginoabdominal examination: a slightly enlarged uterus with a patent external os, and moderate uterine bleeding; ovaries could not be palpated on account of a thick abdominal wall. Two x-rays of the skull at different times showed a normal sella turcica.

*Treatment.*—Having no pathologic report of the curettings obtained six weeks previously, and since the curettage as well as the different endocrine preparations and oxytocic drugs employed failed to stop the uterine bleeding, I advised another diagnostic curettage.

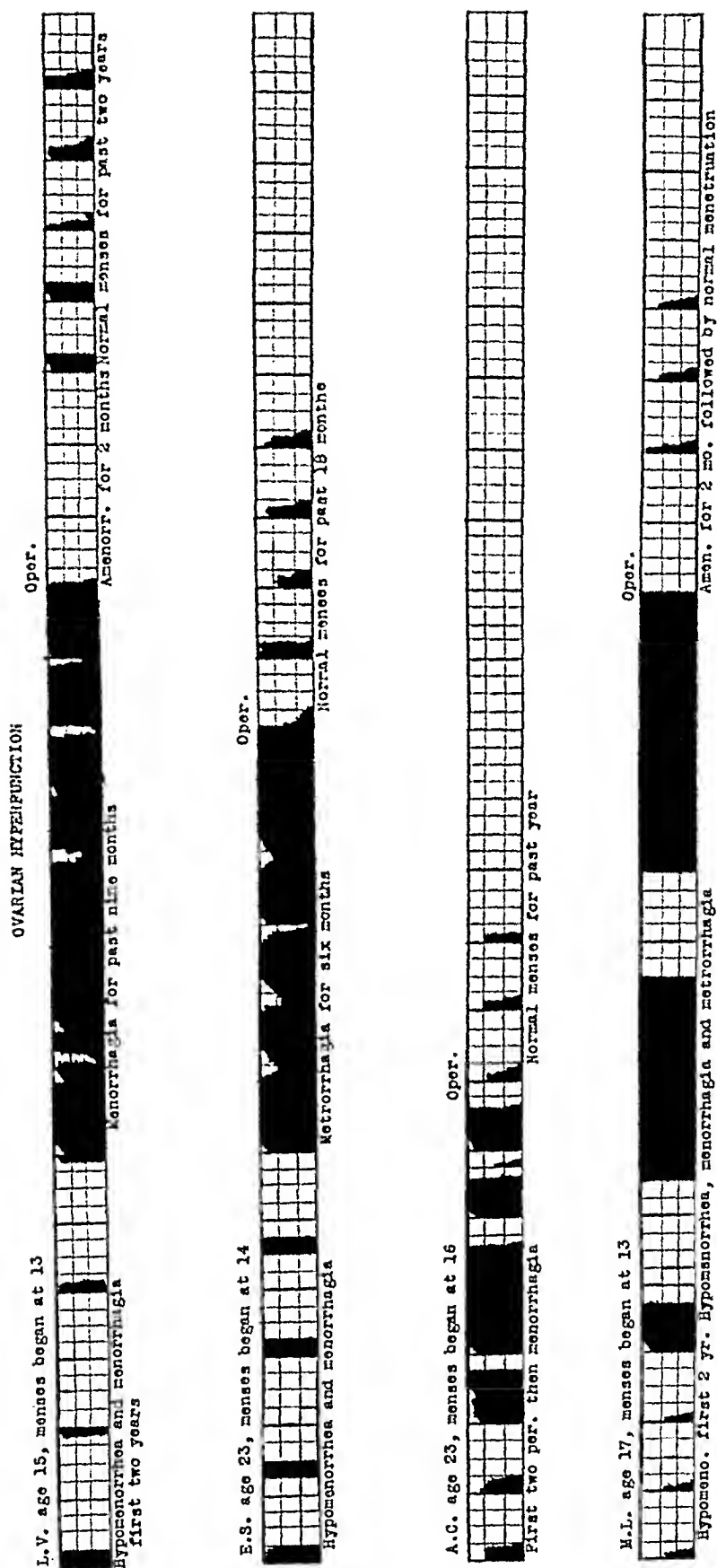


Chart 1.

On May 17, 1932, I performed the second curettage. Uterus measured 9.5 cm. in depth, external os patent, and uterine cavity irregular. An excessive amount of endometrium was recovered. Pathologic report of the curettings: glandular hyperplasia.

As the second curettage also failed to stop the uterine bleeding, and as the cervix remained patent, I suspected in addition to the endocrine dysfunction, also the possibility of a submucous myoma or a polyp, and proposed a more radical procedure.

*Operation.*—On June 2, 1932, laparotomy, a moderately enlarged uterus, soft and regular in outline. Each ovary enlarged to more than twice the normal size, glistening, tense, not adherent, and studded with many microcysts. No gross evidence of a recent corpus luteum. The fallopian tubes normal. An anterior hysterotomy failed to disclose the presence of either a submucous myoma or a polyp. About two-thirds of each ovary was resected in a wedge-shaped form, and the gap closed with a running Cushing-Lambert suture; followed by an appendectomy.

*Pathologic Findings.*—Glandular hyperplasia of the endometrium without a secretory phase. The ovarian tissue was moderately edematous and contained an unusually



Fig. 3.—(Pathol. No. 21,076.) Persistent follicle cyst, marked luteinization of the theca interna (T.I.), granulosa cells (G.C.) not affected. ( $\times 280$ )

large number of atretic follicles in various stages and forms of degeneration (Fig. 2). The cystic follicles were lined with superimposed layers of granulosa cells (Fig. 3) resting upon a luteinized theca interna. One corpus luteum in the stage of proliferation and beginning degeneration was found.

Postoperative clinical course: Since the operation she menstruated normally up to Jan. 9, 1934 (nineteen months).

On March 12, 1934, an intrauterine pregnancy of two months was diagnosed.

On August 1, 1934, she was delivered of a premature stillbirth, breech presentation. On September 14, menses returned and have continued regularly since then.

CASE 3.—Pathol. No. 1103. A. C., aged twenty-three, was admitted to Beth Moses Hospital on Jan. 20, 1933, complaining of menorrhagia, backache, and weakness.

Menses began at sixteen, and after having had two normal menstruations, menorrhagia developed, and since then she flows excessively each month for about twenty days. Any psychic disturbance brings on a uterine flow which lasts for several hours.

*Physical Examination.*—Marked pallor of skin and mucous membranes. Facial and somatic hirsuties, otherwise the secondary sex characteristics are normal. Vagino-pelvic examination; parous vaginal outlet; cervix short, uterus slightly undersized and anteverted. Left adnexa normal to palpation; right ovary enlarged to the size of a small egg, hard in consistency, tender to touch and prolapsed. Hemoglobin 44 per cent; R.B.C. 3,750,000.

*Treatment.*—She was curetted for the menorrhagia in 1925, and again in August, 1932. She also received various medications without avail.

*Operation.*—On Jan. 23, 1933, I performed a total right and a partial left oophorectomy.

*Pathologic Findings.*—A microcystic degeneration of the ovary, some of the cysts measured 8 mm. in diameter. Many old and recent corpora atretica of different sizes appeared as lobulated or strandlike masses of dark or pale pinkish hyaline

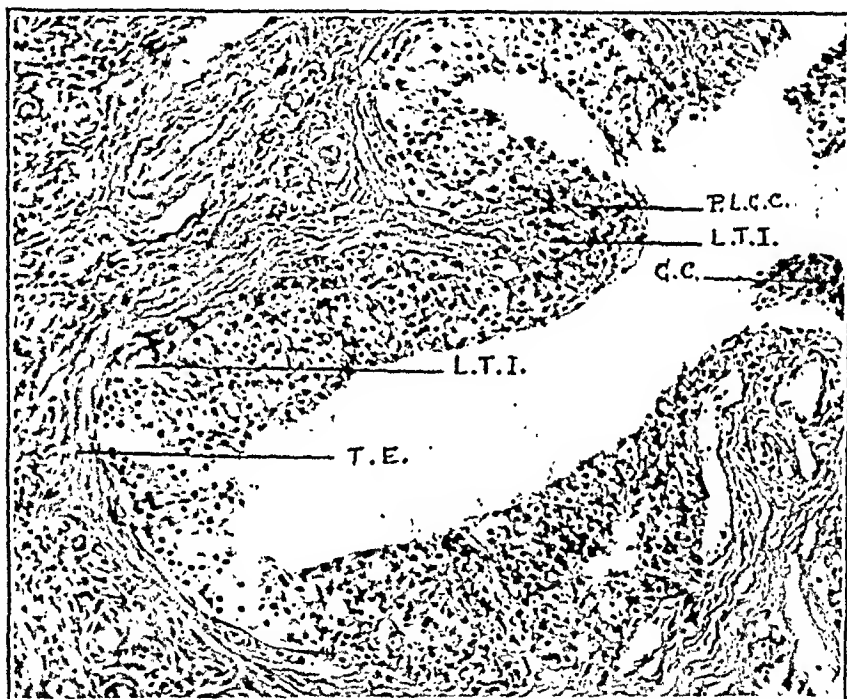


Fig. 4.—(Pathol. No. 1,903) Persistent follicle cyst. Theca externa (T.E.); lutelized theca interna (L.T.I.); nonlutelized granulosa cells (G.C.); pseudoluteinized granulosa cells (P.L.G.C.). ( $\times 240$ )

material. The most recent ones showed young connective tissue in the center. The follicle cysts showed smooth walls; lined with three to four rows of granulosa cells and in many, cumuli were present with or without degenerated ovules. The stroma was normal, and contained too few primordial follicles for her age.

*Postoperative Clinical Course.*—Since the operation, now over one year, her menses are regular, five to six days' duration, and normal in amount. In May, 1934, she was gravid in the fifth month.

CASE 4.—Pathol. No. 1903. M. L., aged seventeen, admitted to Beth Moses Hospital on Aug. 8, 1933, complaining of continuous uterine bleeding for the past four months.

Menses began at 13  $\times$  28  $\times$  3, and continued in this manner for two years. Since her fifteenth year she menstruated at irregular intervals and flowed from three to twelve weeks at a time. For the past four months unremitting uterine bleeding.



*Physical Examination.*—An overdeveloped girl but not disproportionately; primary and secondary sex characteristics normal. Rectopelvic examination disclosed a left cystic ovary somewhat larger than a pigeon's egg. The rest of the generative organs seemed to be normal. Hemoglobin, 50 per cent; R.B.C., 3,260,000; W.B.C., 6,000; no abnormal cells; urine negative.

*Treatment.*—For twelve days intramuscular injections of 1 c.c. of antuitrin-S and 15 gr. of calcium lactate three times daily. In spite of the treatment the bleeding grew worse; the hemoglobin fell to 40 per cent; and the red blood cells to 2,800,000. I then decided to operate.

*Operation.*—The operation, which was preceded by a blood transfusion of 250 c.c., consisted of a curettage, a resection of the cyst-bearing portion of the ovary and an appendectomy. The right ovary although of normal size did not show any evidence of recent ovulation.

*Pathologic Findings.*—Endometrial hyperplasia and cystic dilatation of some glands. No signs of secretory activity. In the stroma a considerable degree of



Fig. 5.—(Pathol. No. 1,903.) Atretic follicle, granulosa cells retaining a normal morphology (G.C.); luteinization of the theca interna (T.I.). (×170)

blood extravasation, and a mononuclear lymphocytic infiltration. The resected ovarian cyst (Fig. 4) showed plications of its walls and marked luteinization of the theca interna, covered with a thick layer of nonluteinized granulosa cells. The luteinization of the theca interna was also noted in the smaller follicle cysts and in many atretic follicles (Fig. 5) in which the granulosa retains its normal morphology.

*Postoperative Clinical Course.*—Immediately following the operation the uterine bleeding ceased, followed by an amenorrhea for seven weeks. Subsequently the menstrual periods became four weekly in type, normal in amount, and have continued in this fashion since then.

#### OVARIAN HYPOFUNCTION

CASE 5.—Pathol. No. 22364 (Beth Israel Hospital). H. M., aged twenty-nine, married two years; nullipara and nulligravida, consulted me on March 8, 1933, complaining of sterility and irregular menstruation.

After her first menstrual period which occurred at the age of sixteen, there followed a period of amenorrhea for two years. Since her eighteenth year the

menstrual intervals have varied from one to three weeks, and the flow from fourteen to twenty days. Ten years ago she was curetted because of menorrhagia. For three months following the curettage, the menses were normal, after which the menorrhagia and the polymenorrhea returned. For the past three years the intermenstrual intervals were prolonged from three to twelve months. The last menstrual period occurred five months ago.

*Physical Examination.*—With the exception of a moderate degree of facial but more marked somatic hirsuties, her other primary and secondary sex characteristics were normal. Both ovaries were enlarged, the left to the size of a chicken's egg, and the right somewhat smaller. The fallopian tubes, apparently normal.

*Operation.*—On March 14, 1933, I performed a curettage and a resection of about two-thirds of each ovary.

*Pathologic Findings.*—Glandular hyperplasia of endometrium (Fig. 6); the lining epithelium was columnar and most of the cells filled with mucus, resembling the interval or the beginning menstrual phase. A marked lymphocytic infiltration of

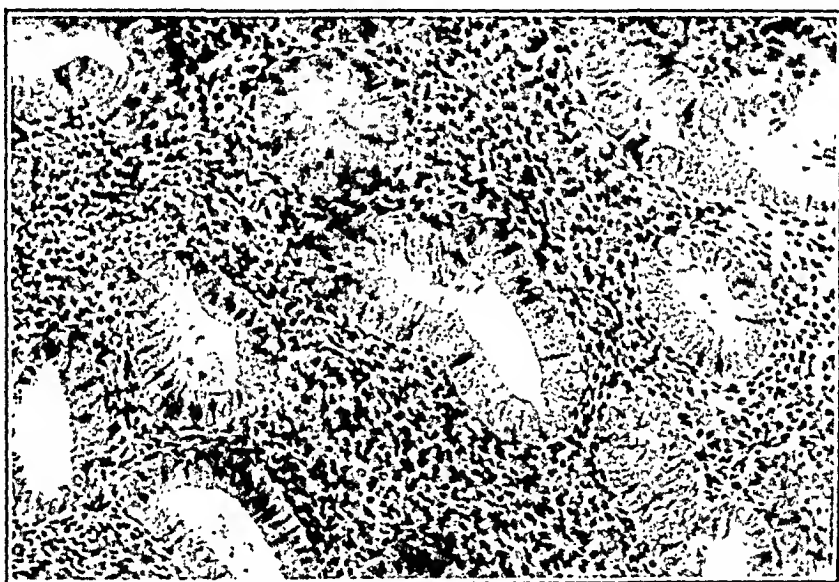


Fig. 6.—(Pathol. No. 22,364.) Endometrium, secretory phase, columnar epithelium and gland lumina filled with mucus, lymphocytic infiltration of stroma. ( $\times 260$ )

the stroma. The ovarian stroma was normal, contained many primary, secondary, and tertiary follicles. No corpora lutea, and only a slight luteinization of the theca interna.

*Postoperative Clinical Course.*—Within one week after the operation the menstrual period had set in, and the flow lasted but three days, instead of the usual three weeks. Since then, now over one year, the sex cycles are normal. On March 4, 1934, she was gravid in the fourth month.

CASE 6.—Pathol. No. 22997 (Beth Israel Hospital). F. R., aged thirty-two, consulted me on July 18, 1933, because of an amenorrhea of one year's duration, intermittent cramplike pains in the lower abdomen for the past few days, and slight vaginal staining.

Menses began at thirteen, always irregular; occurring every two to three months, lasting six to seven days, profuse in amount. For the past three years the menstrual flow was more moderate. The last period had occurred one year previously.

Married twelve years, had given birth to two normal children, the last one seven years ago. She miscarried once, ten years previously.

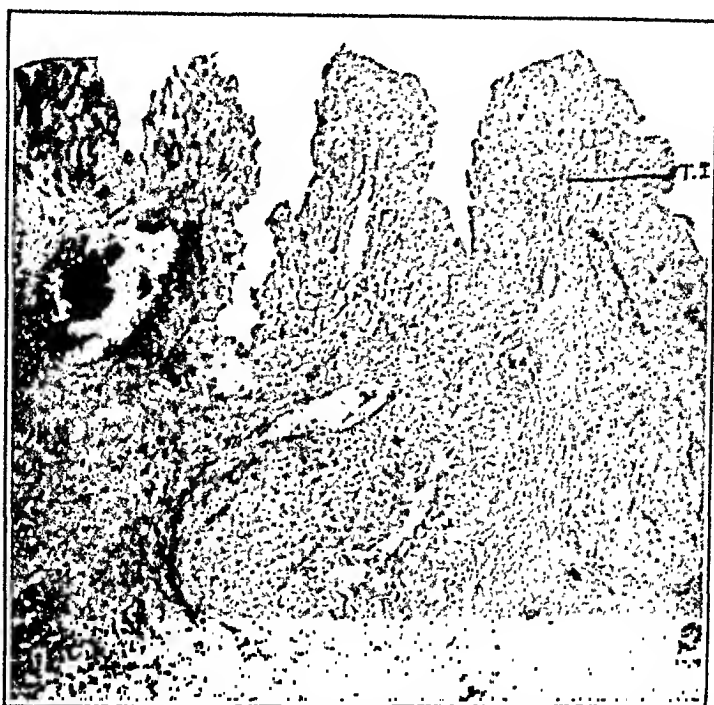


Fig. 7.—(Pathol. No. 22,997.) Persistent corpus luteum cyst, no luteinization of theca interna (T.I.). ( $\times 180$ )



Fig. 8.—(Pathol. No. 22,997.) Secondary follicles undergoing atresia with pronounced luteinization of the granulosa (L.G.); slight luteinization of theca interna (L.T.I.); theca externa (T.E.). ( $\times 160$ )

*Physical Examination.*—A healthy-looking, normally developed female. Vaginal outlet slightly relaxed, uterus normal in size and position. Right ovary enlarged to the size of a small egg, tense, and cystic. The other generative organs apparently normal.

OVARIAN HYPOFUNCTION

H.M. age 29, menses began at 16 followed by amenorrhea for 2 yr.

Polymen. and menorr. Norm. mens. for 3 mo. after C. for first 2 yr.

Polymen. & menorr. for 4 yr. Hypomen. for past 3 yr. intervals. Interv. 4-12 mo.

Oper.

Normal menses for past year

P.R. age 32, mens. began at 13, Grav 111, para 11

Hypomenorrhea

Amenorrhea for one year at the time when applied for treatment

Oper.

On 5th week after oper. normal period and continuing so. Is gravid now.

A.B. age 25, menses began at 13. Sterile

Hypomenorrhea

Oper.

Normal menses since

Chart 2.

*Operation.*—On July 9, 1933, I performed a enucleation and a resection of about two-thirds of each ovary.

*Pathologic Findings.*—Endometrium in a resting state. Ovarian stroma normal; normal proportion of primordial follicles in various stages of degeneration. A persistent corpus luteum cyst (Fig. 7). The follicle cysts were lined with but few rows of granulosa, and very slight luteinization of the theca interna. In some of the secondary follicles the luteinization of the granulosa was quite advanced (Fig. 8).

*Postoperative Clinical Course.*—On Aug. 11, 1933, examination showed normal sized ovaries, freely movable uterus, the amenorrhea still persisting. One hundred R.U. of prolan were administered intramuscularly for six days. Six days later menstruation set in and lasted for five days. On September 26, one intramuscular injection of 100 M.U. of follitropin was administered and on the following day the second menstrual cycle had occurred; it lasted six days. Since then the menses have been normal. On January 8, 1934, she was gravid in the second month.

CASE 7.—Pathol. No. 23,287 (Beth Israel Hospital). A. B., aged twenty-five, married three and a half years, consulted me on Sept. 11, 1933, because of sterility.

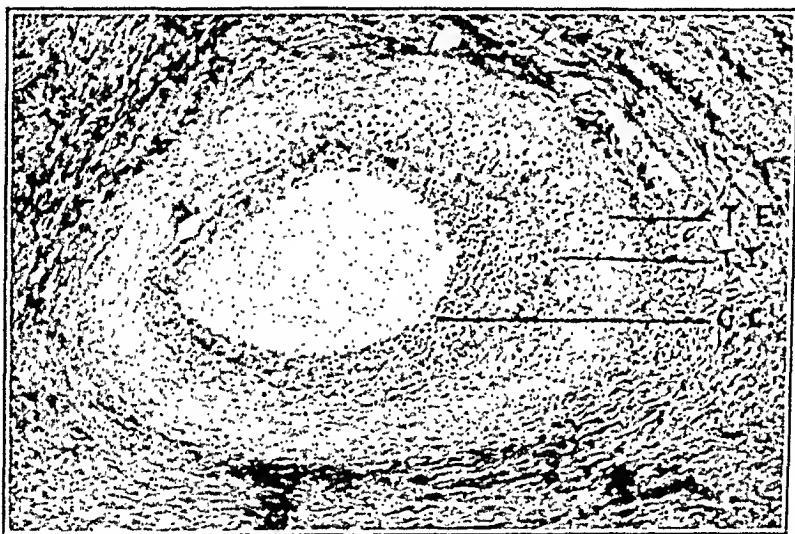


Fig. 9.—(Pathol. No. 23,287.) Secondary follicle undergoing atresia. Theca externa (T.E.): theca interna (T.I.) with marked luteinization; beginning luteinization of the granulosa cells (G.C.). (X160)

Menses began at thirteen, irregular in type, occurring every two, three to five months; six to seven days' duration, profuse in amount and painless. The last menstrual period occurred on Aug. 28, 1933.

*Physical Examination.*—A pronounced somatic and less marked facial hirsuties. Vaginal outlet nulliparous; cervix and uterus were normal. Ovaries enlarged to about two and a half times the normal size, not tender and not adherent. The symphysis pubis was wide and thick, masculine in form.

*Operation.*—On Sept. 23, 1933, I performed a bilateral partial oophorectomy and an appendectomy.

*Pathologic Findings.*—A normal ovarian stroma harboring a quantity of primordial follicles, corresponding to the age of the patient; many of them were degenerated. Also a considerable number of atretic follicles in different stages of involution. The follicle cysts form the prominent pathologic lesion; they were lined with one to three rows of granulosa cells, and their theca interna showed definite luteinization. The lutein conversion of the theca was also noted in the

secondary atretic follicles (Fig. 9), and in some of them the granulosa also showed slight luteinic metaplasia. Only one tertiary follicle was found.

*Postoperative Clinical Course.*—Three days after the operation a menstrual period set in, and the flow lasted four days. This was the first time since puberty that she had had a menstrual interval of only four weeks' duration. For the past six months her menstrual cycles have repeated themselves, every four weeks.

Although I have grouped these cases into two main classifications, a closer study reveals that they can be subdivided into more accurate and more specific groups. It is essential to distinguish between ovarian dysfunctions in which a sex cycle is still preserved, even though imperfect, and those in which it has disappeared. To attain this diagnostic end we must use the normal sex cycle as the standard of comparison for all ovarian dysfunctions.

The biomechanism of a normal sex cycle consists of two phases, a pre- and a postovulatory phase, which occur in rhythmic sequence, each characterized by its hormonal and structural characteristics and clinical manifestations. Comparing ovarian dysfunctions with this physiologic standard, we find that they may be grouped into the following classifications:

1. *Functional Metrorrhagia.*—An arrhythmic dysfunction, characterized by almost continuous uterine bleeding. The chief pathologic changes found were: (a) persistent granulosa cell cysts; (b) extreme luteinization of the theca interna; (c) atretic follicles, in unusually large numbers; (d) small follicle cyst lined with many layers of granulosa; and (e) endometrial hyperplasia. These morphologic findings indicate an uninterrupted overactivity of the first phase of the sex cycle, and an inhibition of the second.

2. *Functional Amenorrhea.*—An arrhythmic dysfunction, characterized by a continued absence of menstruation. In contrast to the sufferers from metrorrhagia these patients feel well and consult us only because they either consider themselves sexually inferior before marriage, or because of sterility or suspected pregnancy thereafter. It is also interesting to note that although this type of amenorrhea may have persisted for a year or more, it is not associated with the vasomotor disturbances characteristic of the natural or the artificial menopause. The main pathologic changes found were: (a) a persistent corpus luteum cyst; (b) a paucity of granulosa cells in the cystic follicles; (c) no, or only slight luteinization of the theca interna; (d) marked luteinization of the granulosa in secondary follicles; and (e) no endometrial hyperplasia. In this type of case the second phase of the sex cycle predominates persistently, and to such an extent that the granulosa is undergoing luteinization before ovulation has taken place.

Both these ovarian dysfunctions, metrorrhagia and total amenorrhea, present an harmonious correlation between their morphology and symptomatology. The reasons for this harmony are quite evident. Just as the pathology in each of them consists of fixed morphologic end-results

of long-standing dysfunctions, so is the resulting symptomatology uniform in nature; acyclical continuous bleeding in the former, and acyclical amenorrhea in the latter.

In between these clear-cut and well-defined types of ovarian dysfunction, we meet with a variety of disorders in which although both phases of the sex cycle are manifest, the functional result is pathologic because the physiologic sequence of the cycles has been disturbed by an untimely occurrence. These types are: functional menorrhagia, polymenorrhea, hypomenorrhea, and oligomenorrhea.

3. *Functional Menorrhagia and Polymenorrhea.*—Both these ovarian dysfunctions are accompanied by a preovulation and a postovulation phase, with the former in the ascendency. The dominance of the first phase is evidenced by the many incompleated ovulations in the form of excessive follicular ripenings, giving rise to an endometrial hyperplasia and hyperemia with excessive menstrual bleeding. We also note premature retrogressions of the ovulating process, in the form of numerous atretic follicles, causing an increase in the number of cycles at the expense of shortened intermenstrual periods.

4. *Functional Hypomenorrhea and Oligomenorrhea.*—In these types of ovarian dysfunction we also note a disturbed rhythm of the sex cycles, with the postovulation phase predominating. The rate of follicle maturation is greatly reduced. The luteinizing effects are quite prominent, as shown by the luteinization of the granulosa cells even before the follicles have ruptured, namely in the secondary stage. In harmony with the morphologic process are the functional results, prolonged intermenstrual intervals, hypomenorrhea; or too little bleeding at the time of menstruation, oligomenorrhea.

The striking difference between menorrhagia, polymenorrhea, hypomenorrhea and oligomenorrhea on the one hand, and metrorrhagia and amenorrhea on the other, is that in the former types of dysfunction, both phases of the cycle are still struggling to regain a balance, while in the latter this struggle is over and only one of the phases rules to the almost complete exclusion of the other. The detection and recognition of this difference is of paramount clinical importance. *I maintain that as long as an ovarian dysfunction still manifests a rhythmical character, broken and distorted as it may be, it is incumbent upon us to persist in opotherapeutic or other nonsurgical methods of treatment; but as soon as the dysfunction becomes devoid of any rhythmic semblance, it indicates that the initial undetectable structural changes within the ovary became definite and fixed lesions, and that the disease has passed from the functional into the organic state, for which partial oophorectomy is thus far the most efficacious remedy.*

The diagrammatic illustration of the beneficial clinical results of partial oophorectomy in ovarian dysfunctions shown in Charts 1 and 2 is so convincing that additional elaboration is unnecessary.

The biochemical investigations of the blood and the urine in cases of ovarian dysfunction by R. T. Frank,<sup>1</sup> and of the hormone content in ovarian tumors by Philipp<sup>2</sup> harmonize with my clinical and pathologic findings, and lend further validity to the axiom that "*all functional disorders have an organic basis.*"

*The Luteinization of the Theca Interna.*—In 1931, Noguehi<sup>3</sup> described this pathologic entity for the first time in hypophysectomized rats injected with pregnancy urine. Seley, Collip and Thompson<sup>4</sup> found a luteinization of the theca interna in sexually immature hypophysectomized rats, when injected with pituitary-like hormone, while the granulosa remained unaltered. In later experiments Collip, Seley, Anderson, and Thompson<sup>5</sup> found that young suckling pigs also responded in a similar manner to injections with pituitary-like hormone.

These investigators claim that the theca interna luteinization observed in the experimental animals is due to the lack of a "complementary substance," which only the pituitary of a normal full-grown animal can produce, and which is not contained in the pituitary-like hormone used in the experiments.

Geist<sup>6</sup> described for the first time (as far as my investigation showed) the luteinization of the theca interna in human beings both after injections with large doses of antuitrin-S, and in four out of twenty-five controls.

I found theca interna luteinization only in ovaries harboring persistent follicle cyst, of much larger dimensions than the ordinary microcystic follicle, with clinical manifestations of ovarian hyperfunction expressing itself in the form of meno- or metrorrhagia of varying rhythm and intensity.

The causal relationship between persistent follicle cysts and increased uterine bleeding of an acyclical form was intimated by August Mayer<sup>7</sup> in 1926. He reasoned thus: "If a persistent corpus luteum cyst leads to an actual amenorrhea, then the opposite ought to result from a persistent follicle cyst." Schroeder,<sup>8</sup> Kermauner,<sup>9</sup> Tietze,<sup>10</sup> and others have proved that this assumption is an actual fact. One of the hiatuses left by the contributors to this subject is the oversight of the morphologic changes in the theca interna. With the exception of Geist, I failed to find a single reference to this structural phenomenon in the human being. I am led to believe from a careful perusal of the literature that persistent follicle cysts with marked luteinization of the theca interna have been mistaken by many for a persistent corpus luteum cyst. As an illustration of this contention I shall cite Tietze very briefly. One of his cases of ovarian hyperfunction with excessive uterine bleeding was eurented. The pathologic report was endometrial hyperplasia. Three weeks later an oophorectomy was performed and the findings were recorded as a persistent corpus luteum cyst. To explain this contradictory pathology the author proffered an ingenious but highly fantastic hypothesis: "Originally we were dealing with a case of large persistent



follicle cyst which became luteinized subsequent to the curettage." I am convinced that Tietze has mistaken the persistent follicle cyst with its luteinized theca interna for a persistent corpus luteum cyst.

To avoid the recurrence of this error I present a composite micrograph (Fig. 10) of a persistent corpus luteum cyst; of a corpus luteum in flower; and of a persistent follicle cyst with a luteinized theca interna. A comparative study of these structures illustrates definitely their morphologic differences.

*What are causal and morphologic correlations between the theca interna luteinization in immature or hypophysectomized rodents injected with pituitary-like hormone; in human beings treated with antuitrin-S;*

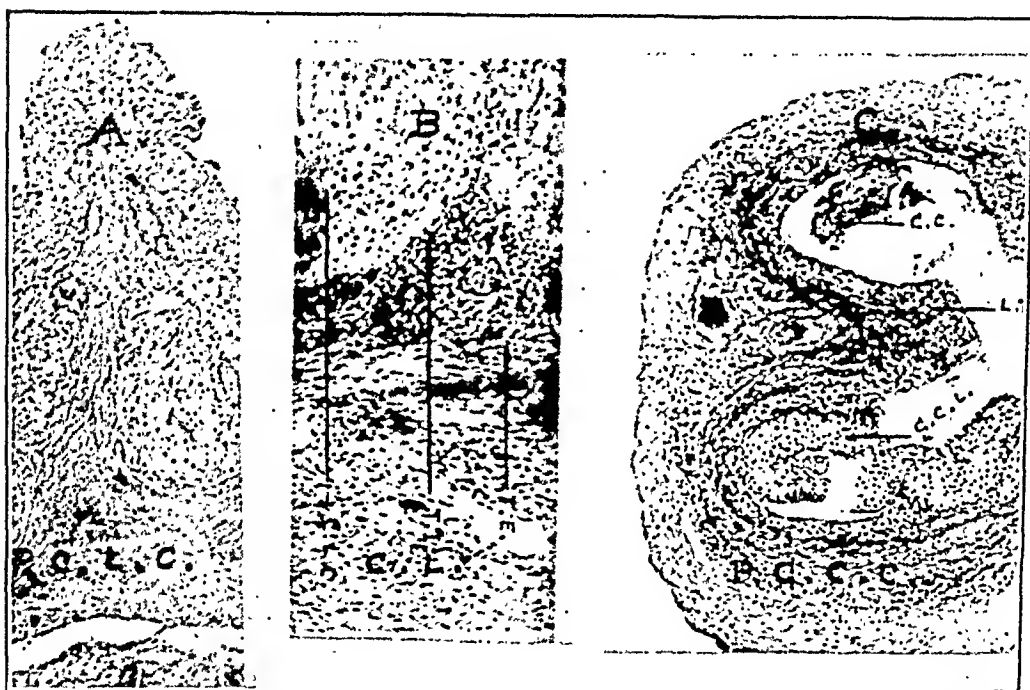


Fig. 10.—A composite photomicrograph of a persistent corpus luteum cyst at A; a normal corpus luteum in flower at B; and a persistent follicle cyst at C. Note the theca interna in the corpus luteum in flower; it consists of round dark staining epithelial cells, resembling the granulosa, cells; in the persistent corpus luteum cyst the theca interna is hardly discernible, while in the persistent follicle cyst the theca interna is extremely luteinized.

*and in human beings suffering from ovarian dysfunctions, particularly of the hyperfunctioning type?* According to Collip and his coworkers, this peculiar response of the ovary is due to the lack of a specific pituitary complement, which he succeeded in isolating. Geist produced a theca interna luteinization in human ovaries with large injections of a pituitary-like hormone. Engle<sup>11</sup> showed definitely that there is a marked difference between pituitary-like substances and the hormone derived from the anterior lobe of the hypophysis. Geist's results must hence be due to the fact that the substance he used lacked that pituitary complement which stands for a normal activation of the ovary. The

spontaneous generation of theca interna luteinization in my cases of ovarian dysfunction must therefore also be due to the same cause, namely an abnormal prolactin secretion.

*How does partial oophorectomy restore the pituitary-ovarian balance?* A comprehensive answer to this question would require a review of the principles governing interglandular correlations in general. Limitation of space in this contribution precludes even the slightest reference to this fascinating problem. It is necessary, however, for our immediate purpose to know at least the essentials of pituitary-ovarian correlations; for without this knowledge no therapeutic measure employed for the correction of an ovarian dysfunction can be undertaken intelligently.

It is now an accepted fact that the pituitary stimulates the ovary, and that the sex gland inhibits the anterior lobe of the hypophysis. As long as these reciprocal stimulations and inhibitions occur in timely and proportionate fashion, so long will the sex cycles run a physiologic course. The moment, however, the balance between the follicle-ripening and the luteinizing hormones of the anterior hypophysis is upset, abnormal structural responses take place in the ovary and in the endometrium, leading to abnormal cyclical or acyclical sex cycles termed ovarian dysfunctions.

In ovarian hyperfunctions the morphologic changes in the sex gland and in the endometrium, as already described in detail, represent the effects of a pituitary hyperstimulation with follicle-ripening hormone. The character and degree of the morphologic responses varies with the phase of the dysfunction. During the early stages when the forces regulating the sex cycles are still attempting to regain their balance, neither the morphologic changes in the ovary, nor the clinical manifestations of the dysfunctions are characterized by uniformity; but later on, when the dysfunction has existed for a long time, both the morphopathology and the symptomatology become fixed and unvarying. It is also to be noted that the more accentuated the follicle-stimulating process is, the more suppressed becomes the luteinizing property of the pituitary; and the more pronounced the granulosa hyperplasia as a result of this type of stimulation, the greater is the ovarian inhibition upon the already weakened luteinizing forces of the hypophysis. A surgical removal of a sufficient amount of ovarian parenchyma harboring an excess of morphologic and biologic elements responsible for the existing functional disturbance, permits the pituitary to regain its intraglandular balance, and thus a restoration of a normal pituitary-ovarian correlation.

In ovarian hypofunctions the reverse holds good. Here the luteinizing forces of the anterior hypophysis play the leading rôle. The morphologic responses to this stimulation are reflected in the ovary and the endometrium. The degree of the structural changes in the ovary and the clinical manifestations of the dysfunction depend upon the

phase of its development. The nearer we approach the terminal phases of the dysfunction the closer does this correlation become, as shown above. The inhibitory effect of the ovary in this type of dysfunction is upon the already weakened follicle-ripening properties of the hypophysis. A removal of a sufficient amount of ovarian parenchyma containing these disturbing elements helps in the restoration of a normal intrahypophyseal balance, and thus a return to a normal pituitary-ovarian correlation.

Since no endocrine function is strictly uniglandular, and since every function of the ductless glands is regulated and controlled by the vegetative nervous system, which is itself activated by the hormones of the endocrines, this study would be incomplete without a very brief allusion to the thyroid and the adrenals, which next to the pituitary, stand in closest functional relationship to the ovary, and to the effect of sympathetic and parasympathetic innervations upon the generative organs.

*The Thyroovarian and the Adrenoovarian Correlations.*—In Breitmänn's<sup>12</sup> scheme of interglandular correlations, which is followed in this study, the thyroid and the adrenals are classified as the stimulators of the ovary, and the ovary as their inhibitor. From clinical observations, experimental studies, and hypotheses bearing on this problem we gather the following information. Thyroxine stimulates the parasympathetic (or vagus), and adrenalin the sympathetic. The parasympathetic fibers (the nervi irrigenti) are the sensory and the vasodilators of the internal and external organs of generation, while the sympathetic (the hypogastrics) are the motor and vasoconstrictor fibers.

Oliver and Schafer<sup>13</sup> have shown (1895) that intravenous injections of thyroid extract caused a fall in blood pressure. The physiologic states in which a drop in blood pressure occurs are the premenstrual and the early gravidity periods which must be due to an increased vagotonia called forth by an increased thyroid activation. Lange<sup>14</sup> observed that women suffering from pregnancy toxemia fail to show the physiologic enlargement of thyroid, and that pregnant animals require more thyroid than nonpregnant in order to remain in a normal state.

Van der Hoeven,<sup>15, 16, 17</sup> as a result of studies of the treatment of pregnancy toxemia and ovarian dysfunctions with thyroid and adrenal extracts, ventured the hypotheses that thyroxine enhances prolactin B elaboration, and adrenalin that of prolactin A. From the experimental researches of Kraul, Hirsch-Hoffman and others (quoted by van der Hoeven), we learn that sympathetic stimulation promotes luteinization, and inhibits follicle maturation; while vagus stimulation hastens follicle ripening, and inhibits luteinization.

I shall now attempt to synthesize all these experimental clinical and hypothetical statements concerning the physiology of the hypophysis, the thyroid, the adrenals, and the vegetative nervous system into an harmonious correlation to ovarian dysfunctions. Before proceeding with this attempt I wish to modify the statement of van der Hoeven "that the thyroid enhances prolactin B secretion, and adrenalin prolactin A" to read "the thyroid inhibits prolactin B elaboration, and the adrenal that of prolactin A." From an endocrinologic standpoint this modification does not

vitiates van der Hoeven's theoretical or therapeutic concepts; but it does sustain the physiologic axiom of interglandular correlations, that no endocrine can return the impulse received to its original source in the same manner. Both the thyroid and the adrenals are stimulated by the hypophysis; they cannot therefore return this stimulating impulse to the hypophysis. The only way in which the thyroid and adrenals can influence the pituitary is in an inhibitory fashion.

In ovarian hyperfunction the follicular apparatus is hyperstimulated by an increase of prolactin A secretion. This heightened pituitary function stimulates the thyroid which leads to an accentuation of vagus innervation. The inhibition of prolactin B by the increase in thyroxine output, and the furthering of prolactin A secretion by the increased vagotonia, represent a harmonious combination of forces and impulses furthering an ovarian dysfunction in which the first phase of the sex cycle predominates. No mention is made of the rôle played by the adrenal because the overwhelming pituitary and thyroid influences suppress to a very large extent its inhibitory effect upon prolactin A production. The statement concerning a greatly diminished adrenal function in this type of ovarian dysfunction is proved clinically by the much reduced sympathicotonia, noted in these patients.

In ovarian hypofunctions the luteinization process in the ovary is markedly pronounced, as a result of an increased prolactin B activation. These cases present abundant clinical evidences of sympathicotonia, which must be due to an increased adrenal function. Increased sympathetic stimulation enhances the process of luteinization, and the increased adrenalemia by further inhibiting the prolactin A production contributes to the prolongation of this form of dysfunction. And just as in the hyperfunctions the thyroid plays the leading supportive rôle, so does the adrenal usurp this rôle in the ovarian hypofunctions. A close clinical observation of patients suffering from ovarian hypofunction furnishes abundant evidences of sympathicotonia.

#### SUMMARY AND CONCLUSIONS

1. Seven cases of ovarian dysfunction were studied clinically and pathologically with the object in view of ascertaining whether functional diseases have an organic basis or not.

2. It was shown that structure and function are indissolubly linked to each other; that the morphologic alterations are almost imperceptible during the early phases of the dysfunction, but that they gain in definiteness and permanence as the dysfunction continues to exist; and that the highest degree of correlation between physiologic and morphologic pathology is noted in the terminal phases of ovarian dysfunctions.

3. An ovarian dysfunction may be considered as having reached the end of its evolution and having merged into a fixed pathologic state when all manifestations of an attempt to return to cyclical functioning have disappeared.

4. As long as cyclical characteristics are still observed in an ovarian dysfunction, we may still pursue nonsurgical therapeutic procedures; but when all palliative measures have been given a fair trial, when all traces of rhythmic functioning have disappeared, and when on bimanual palpation a distinct enlargement of one or both ovaries is established, partial ovarian resection is justified.

5. An adequate analysis and synthesis of the basic endocrinologic principles governing ovarian function and the influence of the vegetative nervous system upon the genital sphere were presented, both of which support the rationality of partial oophorectomy in properly selected cases of ovarian dysfunction.

#### REFERENCES

- (1) *Frank, R. T.*: J. A. M. A. 97: 1852, 1931. (2) *Philipp, E.*: Zentralbl. f. Gynäk. 10: 555, 1934. (3) *Noguchi, Ko.*: Jap. J. Med. Sc. & Pharmacol. 5: 104, 1931. (4) *Seley, H. C., Collip, J. B., and Thompson, D. L.*: Proc. Soc. Exper. Biol. & Med. 30: 780, 1933. (5) *Collip, J. B., Seley, H., Anderson, E. M., and Thompson, D. L.*: J. A. M. A. 101: 1553, 1933. (6) *Geist, S. H.*: AM. J. OBST. & GYNEC. 4: 588, 1933. (7) *Mayer, A.*: Klinik der Ovarialtumor, Halbon und Seitz. Biologie u. Pathologie des Weibes, Vol. 52. (8) *Schroeder, R.*: Handb. d. Gynäk. 1: 306, 1928. (9) *Kermauner, F.*: Veit-Stoeckel Handb. d. Gynäk. 7: 1932. (10) *Tietze, K.*: Arch. f. Gynäk. 155: 525, 1934. (11) *Engle, E. T.*: Proc. Soc. Exper. Biol. & Med. 30: 530, 1933. (12) *Breitmann*: Handb. der inn. sekret. 3: I Berlin, 1933. (13) *Oliver, G., and Schafer, E. A.*: J. Physiol. 18: 230, 1895. (14) *Lange*: Ztschr. f. Geburtsh. u. Gynäk. 40: 1, 1899. (15) *Van der Hoeven, H.*: Ztschr. f. Geburtsh. 104: 337, 1933. (16) *Idem*: Zentralbl. f. Gynäk. 24: 1405, 1934. (17) *Idem*: Zentralbl. f. Gynäk. 5: 928, 1934.

---

**Davidson, A. H.**: Ovarian Conditions as Causes of Pelvic Pain, Brit. M. J. 2: 623, 1934.

In the opinion of the author, conservatism is the keynote to be adopted when surgical removal of the ovaries is being considered for various vague pelvic pains. Taking a clinical approach to the subject, he stresses the necessity of physical signs being elicited in the ovary or its neighborhood before blaming it as a cause of pain.

Ovaries which are the seat of chronic infection are usually best treated by clearing up the pelvis, returning the organs to as normal a position as possible and removing what is beyond repair. Prolapsed ovaries, with or without associated retroflexed uteri, are mentioned as causes of pelvic pain. The treatment of this condition is restoration of the organs to as normal a position as possible.

Endometriomas, often with ovarian dysmenorrhea, may cause pain, especially in women over thirty. The author professes little belief in the idea that small cystic ovaries or cirrhotic ovaries are pathologic entities causing pain.

Mention is made of three conditions which have been wrongfully dubbed ovarian pain: (a) reflected pain, (b) neurasthenic pain, and (c) hysterical pain.

In conclusion, the author advises careful examination for definite physical signs of pathology in the genitalia, if necessary under an anesthetic when a Rubin's test may also be carried out, and if no pathologic condition can be found, the patient should be dissuaded from operation and put on general medical management.

## THE MANAGEMENT OF THE PRENATAL AND THE POSTNATAL CERVIX

MARIO A. CASTALLO, M.D., AND THADDEUS L. MONTGOMERY, M.D.,  
PHILADELPHIA, PA.

*(From the Department of Obstetrics, Jefferson Medical College Hospital)*

THE purpose of this presentation is to discuss the problems of cervical disease as they are met in obstetric practice, and to define the responsibilities of the obstetrician who has to deal with them. The substance of the paper is based upon observations which have been conducted in the department of obstetrics of the Jefferson Medical College Hospital during a nine-year period. Contributions that have been made by this clinic to the study of cervical pathology from time to time are incorporated, and the methods of treatment that are now in vogue are described.

The two types of cervical disease which concern the obstetrician in modern day practice are the inflammatory and the precancerous, or cancer predisposing. Of the two, the inflammatory lesions are a particular consideration of the antenatal period and the cancer predisposing of the postnatal.

In a publication five years ago, Dr. J. Bernard Bernstein and one of us (Montgomery) discussed the importance of cervical infection in obstetrics and presented the results which were obtained from 1925 to 1928 in a special clinic for the treatment of gonorrhea complicating pregnancy. The results proved quite satisfactory in the lowering of puerperal morbidity and in the lessening of ophthalmia neonatorum. An outstanding feature of the study was the proof that the cervix can be treated without danger to the mother or to the embryo. Abortion, miscarriage, and premature labor occurred no more frequently among the treated patients than in the others of the service. These findings encouraged us to continue with our efforts to treat cervical inflammation of this type and better prepare the birth canal for delivery.

A recent review of our statistics reveals that from 1928 to 1932 the laboratory diagnosis of gonorrhea (positive smear) was made in 84 of the 3,586 patients who were later delivered under our supervision. In no instance among these 84 patients treated for gonorrhea complicating pregnancy did ophthalmia neonatorum occur in the newborn. During the same time there were fifteen cases in the nontreated patients. In two of the 84 treated patients pregnancy terminated prematurely, once by abortion and once by premature labor.

We concluded that it is decidedly worth while to treat these patients during the course of pregnancy, that the treatment, while not expected to cure the cervical disease, allays the inflammation and prepares the birth canal for labor and the puerperal period.

#### METHOD

The treatment consists of certain measures which are performed by the patient in her home, and others which are conducted in the antenatal clinic. The home care consists of a daily Lugol's solution douche (1 teaspoonful of liquor iodi compositus to 2 quarts of warm boiled water) administered through a carefully prepared douche apparatus. Upon retiring the patient inserts a medicated vaginal suppository consisting of 4 per cent powdered mercurochrome in a cacao butter base. This suppository is allowed to liquefy in the vaginal tract and remain until the next douche is administered. Upon the weekly visit at the clinic the cervix is exposed, cleansed with an alkaline antiseptic, and painted with a 5 per cent watery solution of mercurochrome or a 1:1000 watery solution of metaphen. The solution is carried with a swab well up into the cervical canal. With a second small swab it is instilled in the anterior portion of the urethra. If the granulations of an ulcerated cervix are effusive, they are touched up lightly with the electric cautery.

We have no hesitancy in applying this same treatment to the non-specific infections of the cervix in pregnancy. Any doubt as to the infective nature of these lesions is dispelled by histologic study of the involved tissue. In 20 instances we collected tissue for biopsy from cervixes of this type. Examination of the histologic sections revealed in each instance desquamation of the squamous epithelium, purulent fluid exuding from the cervical glands, and an extensive leucocytic infiltration of the adjacent cervical stroma. The picture is that of an open ulcer (Figs. 1 and 2).

These nonspecific infections of the cervix challenge the watchfulness of the obstetrician and also call for active treatment. In such instances more reliance is to be placed upon the prenatal care than upon the practice of trying to sterilize the birth canal at the time of labor. While not in any way minimizing the importance of careful antiseptic preparation of the birth canal at the time of delivery, it is so obviously impossible to carry medication into the infected lumina of the cervical glands that the practice of repeatedly instilling antiseptics into the vaginal tract during the course of labor and especially of massaging them into the cervix appears not only futile but also not entirely devoid of danger.

The paramount concern of the labor period is careful management and conservation of the defensive forces of the patient. Of particular importance to this end are the following points: first, preservation of the membranes and noninterference in the stage of dilating, a strict policy of "hands off" during the time that nature is gently thinning and dilating the cervix; second, a reasonably prompt delivery of the fetus when the stage of dilatation is completed; third, careful atten-

tion to the placental stage with prompt expulsion of that organ when it has separated from the wall of the uterus, a policy which calls for arrest of anesthesia and postponement of repair until the third stage is completed and the empty uterus firmly retracted; fourth, tampon-

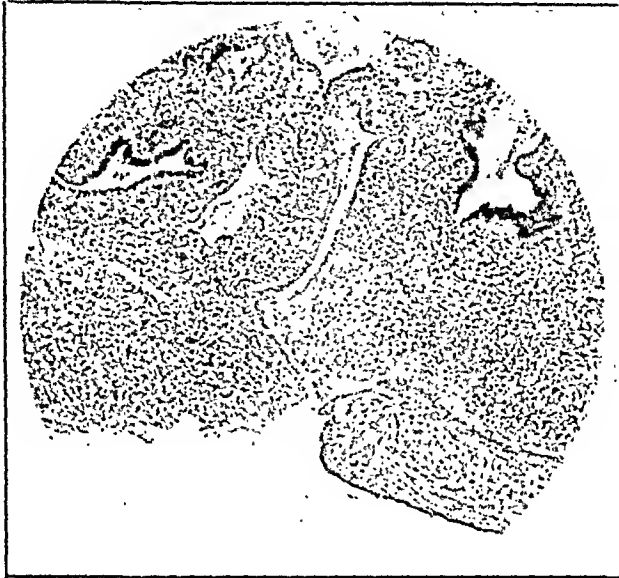


Fig. 1.—Acute ulcerative endocervicitis complicating pregnancy. Note the loss of squamous epithelium, the pus exuding from the cervical gland, the extensive leucocytic exudate in the stroma. (Photomicrograph 60X.)



Fig. 2.—Acute ulcerative endocervicitis complicating pregnancy. Higher power magnification taken at the ostium of the cervical gland in Fig. 1. (Photomicrograph 220X.)

age of the uterus whenever that organ fails to contract properly or when moderate bleeding occurs; fifth, avoidance of exposure or manipulation of the cervix after delivery except for the purpose of arresting traumatic hemorrhage.



We have been particularly interested in the effect that premature rupture of the membranes and prolonged labor have upon the convalescence of mother and baby after delivery. The influence of these conditions upon the production of postpartum endometritis and puer-



Fig. 3.—Acute inflammation of the margin of the placenta. Light leucocytic infiltration extending from the membranes to the corresponding layers of the margin of the placenta. (Photomicrograph 57 $\times$ .)

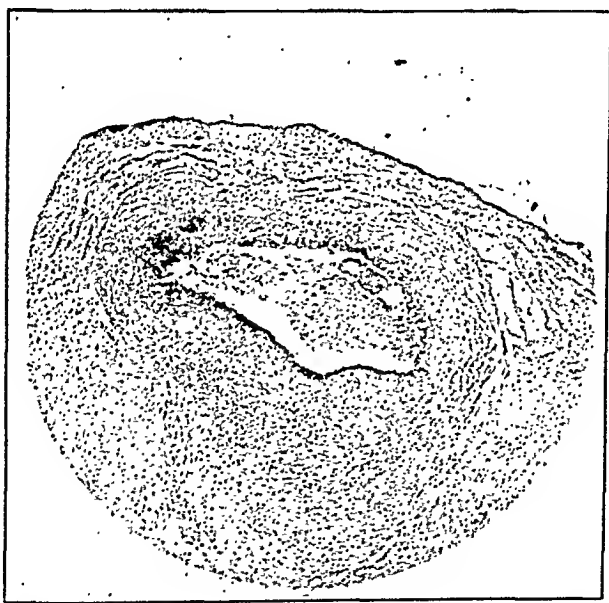


Fig. 4.—Acute inflammation of a large placental vessel. Leucocytic infiltration of the intima, the muscle wall, and the perivascular tissue of one of the large veins on the fetal surface of the placenta. (Photomicrograph 40 $\times$ .)

peral morbidity has been frequently emphasized, but the part they play in creating lesions of the placenta and fetal circulation has not been so well recognized.

Significant contributions in the latter field have been made by Warnekros, Siddall, Slemons, and others. The attention of one of us (Montgomery) was directed to the problem during the course of a histologic study of 650 freshly delivered placentas. In 67 specimens of this group (10 per cent) acute inflammatory lesions were found. The inflammatory reaction apparently develops during the course of labor and is associated particularly with instances of premature rupture of the membranes, prolonged labor, and difficult operations of vaginal delivery. The infection apparently begins in the membranes at the margin of the cervical aperture, ascends to the edge of the placenta (Fig. 3), is taken up by the fetal vessels of the placenta (Fig. 4), gives rise not infrequently to thrombophlebitis of the cord vein (Fig. 5).



Fig. 5.—Acute thrombophlebitis of cord vein. Leucocytic infiltration in the interstices of the muscle wall and intima. Meshwork of fibrin and leucocytes projecting into the vessel lumen.

As a result of this infection of placental vessels, fetal bacteremia may develop (Kobak) and neonatal illness or death occur.

The manner in which the inflammatory lesion starts at the margin of the cervical aperture emphasizes again the importance of the cervix as an etiologic focus of disease.

#### CANCER PREDISPOSING LESIONS

The conclusion of labor terminates the obstetrician's chance to forestall the ravages of cervical infection. The patient's fate, thenceforth, depends upon the strength of her resistance and upon the virulence of the bacteria which inhabit her birth canal.

The attention of the physician is now directed to measures of restoration, restoration of the pelvic floor and perineum to their cus-

tomary configuration, and particularly of the cervix to a normal nulliparous-like contour. To precisely the same degree that prenatal treatment of the infected cervix is necessary for the prevention of puerperal infection, so also is postnatal restoration of the cervix required for the prevention of cervical cancer.

If one could safely and satisfactorily expose and suture the cervix after delivery, primary repair of this channel would be the method of choice. However, it has been our experience that such unwarranted risks are taken in the exposure and manipulation of the cervix immediately after delivery that more is lost in the routine application of this procedure than is gained in the few cases that are found to require suture. We find very few cases of extensive cervical damage when the course of labor has been properly conducted. Our immediate repair of the birth canal is limited, therefore, to the vaginal wall and perineum unless traumatic hemorrhage calls for suturing at higher levels.

To the minor degrees of cervical trauma, treatment with the electric cautery during the postnatal period is particularly applicable. The application is made at first rather lightly on the sixth or eighth week postpartum. The treatment is repeated every three weeks until all areas of laceration and erosion are epithelialized. An alternate method of dealing with these lesions is the conization method of Hyams.

More extensive degrees of cervical damage are amenable to correction by intermediate or secondary repair. The intermediate repair may be performed on the fifth to the eighth day of the puerperium, depending upon the speed of the patient's convalescence. The result of the repair of the succulent puerperal cervix is quite satisfactory. The operation is often followed by a morbid temperature reaction, however, and the stay in the hospital is considerably prolonged. Repair performed several months after delivery, secondary repair, is the safest and best method of correcting extensive cervical damage. For this purpose patients are readmitted to the hospital after the period of lactation is completed.

It is now recognized that the obstetrician in his follow-up examination of the obstetric patient and in his program of annual health examinations has an excellent opportunity to make the early diagnosis of cervical malignancy. Certainly he has it within his power to educate his patients in the importance of annual health examinations. These annual health examinations have become of greater significance as more scientific methods of study have been devised. Particularly is this true in the detection of cervical pathology. The findings of pelvic examination have not been hitherto completely satisfactory. Lesions have been detected only in their fully developed state. As a result, out of five women upon whom a diagnosis of carcinoma of the cervix is made, four die within five years.

It is now agreed that if we are to lower the mortality rate from carcinoma of the cervix, it will have to be done by making the diagnosis earlier, and by prophylactic measures. Surgery and radium in the treatment of this disease entity seemingly have reached their height of usefulness. In spite of propaganda to the laity, and the furtherance of the regular medical examinations, there has been no appreciable reduction of the death rate. While it is true that more and more cases are being diagnosed than there were ten years ago, nevertheless they are being seen too late for effective treatment to alter materially the percentage of cures.

It has been said that a latent period of carcinoma extends over a period of years before the disease becomes a clinically demonstrable entity. Bland states that mice subjected to long-continued irritation by tar will develop newgrowths in about six months, one-sixth the normal span of a mouse's life. Applied to man, this would correspond to from ten to fifteen years. This statement is supported by observations on occupational carcinoma, which do not manifest themselves until ten to fifteen years after the occupation has been started.

Periodic vaginal examinations, as they are done today, and biopsy of the cervix are doing much to bring individuals to early treatment. As a rule, however, it is not early enough. If we are to detect the small areas of early carcinoma which are present before ulceration occurs, we must look to methods not in general use. To this end Hinselmann designed the "colposcope" and reported upon its use in 1928. Closely following this treatise Schiller advocated the use of Lugol's solution for the detection of clinically undistinguishable carcinoma of the cervix. By these methods, it is claimed, a suspicious area is more easily detected, and biopsy more accurately procured.

#### TECHNIC OF TEST

We began the study of the cervix with the Schiller test some five months ago. After experimenting with the colposcope, various types of lenses and binoculars suggested by Hirst, we developed the following procedures:

A preliminary examination is made without lubricating the fingers, and a speculum is inserted without the use of lubricants. The cervix is wiped clean of mucus with a swab of absorbent cotton, care being taken not to traumatize the epithelium. The same type swab is immersed in full strength Lugol's solution (other dilutions have been tried without the same degree of success) and the entire cervix is bathed, making sure that the surrounding areas are included. Especially are we careful to distend the folds surrounding the cervix so that the entire area is well stained. After a minute the excess is removed with absorbent cotton. The magnifying apparatus is then set up and the cervical epithelium inspected. Biopsy is taken from stain deficient areas. For this purpose the cutting current loop is particularly well adapted. Bleeding is arrested by electrocoagulation or with the cautery.

If the cervix is examined without previous staining, any area which presents a dull, opaque, or wrinkled appearance against the normal glistening surface of the epithelium is the point at which a biopsy is taken.

Schiller advocates taking for diagnosis only a small piece of the surface epithelium. For this purpose he uses a spoon curette. He contends that the slightest change in the morphology of the epithelial cells is so characteristic that the diagnosis of carcinoma may be made from it alone. Other pathologists, including Dr. Baxter Crawford, do not agree with this view, contending that it is too meager a criterion.

Dr. Crawford states that a diagnosis of carcinoma cannot be made unless there is invasion of the basement membrane. For this reason we take a generous biopsy which dips into the underlying musculature.

Every postpartum cervix is examined by either or both of the above mentioned methods. Any cervix which appears abnormal during the antenatal examination is also referred for study. Contraindications to the use of the Schiller test and the colposcopic examinations are not often mentioned. If there is acute infection of the vaginal vault, puerperal bleeding, infection in the pelvis, or any gross pathology of the vagina or cervix, we deem it better not to make the test until a later date.

#### REPORT OF CASES

Total number of cases tested	109
Primigravida	30
Multigravida	79
Oldest	44
Youngest	15
Largest age group	20-35 years
Type of last delivery	
Spontaneous	96
Operative vaginal delivery	9
Caesarean Section	3
Number positive Schiller tests	15
Of the positive Schiller group	
Primigravida	0
Multigravida	15
Youngest	21
Oldest	44
Between 20-30	9
Between 30-40	3
Over 40	3
Biopsies taken	15
Biopsy report	
Chronic cervicitis	3
Thickened epith. surface	3
Hyperkeratosis	6
Keratinized areas	2
Fibroglandular polyps cervix (Fig. 9)	1
Treatment used	
Electric cautery	103
50 per cent silver nitrate	2
No treatment	4

It is our custom to have the parturient return for her first postpartum examination six weeks after delivery. At this time the usual postnatal examination is made and the patient is directed to return in one month. At the second visit the Schiller test and colposcopic examination are performed. Most patients require

some form of treatment of the cervix. The Schiller test and colposcopic examination performed at the sixth week postpartum are distorted by the edema and the results are not completely satisfactory.

Although no instances of early malignancy have as yet been discovered, this method of examination has disclosed a number of important lesions. We feel that progress has been made in the treatment of the postnatal cervix, and that these special studies fully justify the time and attention which are devoted to them.

#### SUMMARY

A résumé of the management and treatment of the cervical lesions which complicate obstetric practice has been presented. The responsibilities of the obstetrician in this connection have been pointed out. Special attention has been directed to six points:

1. The importance of detecting cervical infection and recognizing its etiologic relationship to puerperal infection.
2. The efficacy and safety of treatment of the cervix during the period of pregnancy.
3. The necessity of pursuing a conservative and thoughtful plan of tactics during the course of labor.
4. The rôle of the obstetrician in restoring the birth canal to natural contour and integument.
5. The importance of cauterization treatment or, when indicated, of operative repair during the postnatal period.
6. The value and the method of application of new methods of diagnosis in early carcinoma of the cervix.

The authors wish to express their gratitude to Dr. P. Brooke Bland for his interest and material help in carrying on these studies. They are also deeply indebted to Dr. Baxter Crawford and the personnel of the hospital laboratories for their valued contributions in the study of pathologic material.

#### REFERENCES

- Bernstine, J. B., and Montgomery, T. L.*: J. Urol. 22: 420, 1928. *Bland, P. Brooke*: N. E. J. Med. 202: 1195, 1930. *Davis, J. E.*: Am. J. Surg. 17: 32, 1932. *Graves, W. P.*: Surg. Gynec. Obst. 56: 317, 1933. *Hinselmann, H.*: Chirurg. 2: 549, 1930. *Hirst, B. C.*: J. A. M. A. 101: 897, 1933. *Kobak, M. S.*: AM. J. OBST. & GYNEC. 19: 299, 1930. *Montgomery, T. L.*: AM. J. OBST. & GYNEC. 25: 320, 1933. *Preissecker, E.*: Wien. klin. Wchnschr. 42: 1352, 1929. *Schiller, W.*: Zentralbl. f. Gynäk. 53: 1056, 1929. *Schiller, W.*: Surg. Gynec. Obst. 56: 210, 1933. *Siddall, R. S.*: AM. J. OBST. & GYNEC. (In Press.) *Slemons, J. Morris*: J. A. M. A. 45: 1265, 1915. *Wohlwill, Friedrich, and Bock, Hans Ehard*: Beitr. z. Path. Anat. u. z. Allg. Path. 85: 469, 1930.

248 SOUTH TWENTY-FIRST STREET  
1930 CHESTNUT STREET

## VERATRUM VIRIDE IN THE TREATMENT OF ECLAMPSIA

RICHARD D. BRYANT, M.D., CINCINNATI, OHIO

*(From the Department of Obstetrics of the College of Medicine of the University of Cincinnati and the Cincinnati General Hospital)*

NOTWITHSTANDING the great strides made in recent years toward reducing both the frequency and the severity of the "toxemias" of late pregnancy, they are still met with only too often, and exact a toll much too large from childbearing women. The most dramatic, and at the same time the most severe, type of "toxemia" is eclampsia. Recent mortality statistics show that eclampsia and other toxemias of late pregnancy rank along with sepsis as a cause of maternal deaths. DeLee<sup>1</sup> says: "Over 20 per cent of women afflicted with eclampsia die, and this has been hardly affected by changes of treatment in the last hundred years." Williams<sup>2</sup> places the figure at 20 to 25 per cent. However, most large clinics today report much better results than this.

At present the majority of systems of treatment of eclampsia are based upon either the Dublin or the Stroganoff method. Lazard<sup>3</sup> has treated a large series of cases with intravenous administration of magnesium sulphate with comparatively good results. A quarter of a century ago veratrum viride was considered as almost specific in some parts of the country, but fell into disrepute because it was abused. However, veratrum viride (under the trade name Veratrone—Parke, Davis & Co.) has been the basis of the treatment of eclampsia at the Cincinnati General Hospital for many years. The method of treatment has been modified from time to time as new therapeutic agents were introduced, but has remained nearly the same for the last eight years. The results have been so satisfactory, when compared with results obtained with other methods of treatment, that it is felt they are worth reporting, along with an outline of the treatment used.

The cases reported in this series are consecutive cases of so-called eclampsia. The diagnosis was based upon the following points: (1) Pregnancy of at least five months' duration, or pregnancy of at least five months' duration terminated no more than ten days before the first convulsion; (2) hypertension; (3) albuminuria; (4) convulsions, or history of convulsions, as many patients were not actually seen in the convulsive seizures; and (5) coma following the convulsions.

### TREATMENT

The treatment was as follows: (1) Veratrum viride, by mouth, by hypo, or both; (2) magnesium sulphate, 50 per cent solution, intramus-

cularly; (3) magnesium sulphate by mouth; (4) forcing of fluids, by mouth, hypodermoclysis, or intravenous injection; (5) alkalis by mouth, sodium bicarbonate and sodium citrate; (6) low protein diet; (7) sedatives as needed for restlessness, analgesics and anodynes during labor, as needed; and (8) in the predelivery cases, treating the pregnancy conservatively.

1. "Veratrone," 5 to 15 minims by hypo or deep injection is given as soon after the first convulsion as possible. This is repeated as often as is necessary to keep the pulse below 80, or the blood pressure at least 20 mm. below the convulsive level. The usual case requires one to three doses at ten- to fifteen-minute intervals, then doses every one, two, or three hours until the patient is well over the acute stage. Oral administration of slightly larger doses, 10 to 20 minims, may replace the hypodermic injections as the patient recovers.

2. Magnesium sulphate, 50 per cent solution, 10 to 20 c.c. is given by deep injection immediately following the first dose of veratrone. This is repeated in smaller doses, 2 to 5 c.c., every six hours, three times a day, and twice a day, on successive days, as the acute attack subsides.

3. One-half to one ounce of saturated solution of magnesium sulphate is given by mouth twice a day.

4. Fluids are forced by mouth as soon as the patient is conscious. In the meantime 2,000 to 3,000 c.c. of saline are given by hypodermoclysis if the patient is over the convulsive stage but still comatose. Intravenous injection of 100 to 500 c.c. of glucose, 5 to 50 per cent, is frequently used.

5. Alkalis are given by mouth to conscious patients in doses of 60 to 120 gr. three to six times a day. Fruit juices, well sweetened, are administered at frequent intervals, when the patient can be aroused enough to drink.

6. A low protein diet, consisting chiefly of fruit juices, vegetables and bread, is allowed as soon as the patient feels hungry, and is apparently in no immediate danger of convulsions.

7. Chloral, bromides, or one of the barbiturates are given in appropriate doses to those patients who become restless during recovery from the acute stage. A modified Gwathmey technic is used during labor. Ether is used sparingly at the time of delivery.

8. In the antepartal case, no attempt is made to induce labor until the patient is well over the acute stage, or shows marked resistance to treatment. In the patient who responds to treatment, labor is induced twenty-four to seventy-two hours after the acute attack has subsided. In this series of cases there were seventy-one patients with convulsions before delivery. The types of induction used in these patients were as follows:

No induction needed	34
Braun bag	19
Castor oil and quinine	5
Digital "stripping membranes"	4
Rupture of membranes	1
Castor oil only	1
Castor oil and quinine, followed by bag	1
Cervix packed	1
Died undelivered	5
	<hr/>
	71



The methods of delivery in the predelivery cases were as follows:

Spontaneous delivery	38
Low forceps	12
Midforceps	4
High forceps	1
Scanzoni	2
Breech	5
Version and extraction	4
Postmortem cesarean section	2
Died undelivered	3
	<hr/> 71

Pitocin is used as the abolic after the completion of the third stage of labor.

The usual precautions are used during the convulsions. Biting of the tongue is prevented by a suitably padded gag. The throat is kept free of mucus. The patient is not restrained during a convulsion, except so far as is needed to prevent self-injury by falling or striking the bedposts. No anesthetic is used for the control of the convulsions. Acute cardiac failure is the only indication for venesection. A catheterized urine specimen is obtained as soon as practical. A large soap water enema is given as soon as the patient can cooperate.

An occasional patient was subjected to spinal puncture. In three cases, magnesium sulphate solution was injected intraspinally. Two patients received magnesium sulphate solution intravenously. It is felt that colonic irrigations are of distinct value in certain types of cases, but because of limited nursing facilities this procedure has not been carried out routinely. Because of circumstances, none of these patients were isolated, but were kept on the open thirty-bed ward, under the observation of internes, and general duty and student nurses. Pulse and blood pressure readings are taken at frequent intervals, and any sign of impending convulsions is carefully investigated.

#### RATIONALE OF THERAPY

1. The cause of eclampsia is, of course, the products of conception, since eclampsia gravidarum, by definition, never occurs in the absence of conception. How the products of conception produce eclampsia is wholly unknown. Many theories have been advanced to explain the phenomenon, and new theories are reported almost yearly. Yet all that can be demonstrated unequivocally are the results of the "toxemia."

Hypertension is one of the outstanding and constant clinical findings in eclampsia. It is a sign of increased vasoconstriction. Theoretical evidence of this is offered by Fishberg<sup>1</sup> when he says that "... the only mechanism of protracted hypertension that harmonizes with the known facts, and has a sound physiologic basis, is a widespread or perhaps universal increase in the tonus of the arterioles." On the clinical side Haselhorst and Mylius<sup>5</sup> have seen and photographed intermittent and sustained abnormal constriction of the blood vessels of the retina. The cause of the vasoconstriction is, directly or indirectly, the cause of eclampsia. This excessive vasoconstriction may possibly be caused by hyperfunctioning of the postpituitary, as suggested by Hofbauer in 1918,<sup>6</sup> and reiterated in 1933.<sup>7</sup> The work of Anselmino, Hoffmann, and Kennedy<sup>8</sup> and others seem to lend support to this theory. At any rate

the vasoconstriction gives rise to a train of pathologic events. A hypertension develops which throws an added strain on the heart and blood vessels, either of which may give way, with disastrous results. Furthermore, the vasoconstriction itself, we may postulate, leads to anemia of the tissues, with suboxidation, retention of waste products of metabolism, and eventually edema. The edema, by pressure, leads to further vasoconstriction. Thus a vicious cycle is established.

This vicious cycle must be interrupted at some point. In this series, this has been accomplished with veratrine. That veratrum viride has a vasodilating action is attested by Cramer,<sup>9</sup> who says: "Veratrum viride is therapeutically valuable, as in suitable doses it affords a means of producing a lasting vasodilatation through acting reflexly on the vasomotor center." Solis-Cohen and Githens<sup>10</sup> and Hare<sup>11</sup> also agree that there is a vasodilatation produced by the drug. This vasodilatation apparently results in an increased blood supply to the various organs. This encourages a more normal exchange of metabolites and at the same time allows more ready access of drugs such as dehydrators and alkalies. The edema of the brain, skin, and kidneys diminishes, so that cessation of convulsions, return of consciousness, diuresis, and diaphoresis result. Other effects of the drug, lowering of the blood pressure, slowing of the heartbeat and respiration, diarrhea, and vomiting, although marked and even alarming at times, are apparently harmless. The vomiting in particular is probably of definite value, as the loss of HCl tends to diminish the ever-present acidosis. It is certain that the benefits of the drug far outweigh these temporary disadvantages.

2. Magnesium sulphate by deep injection is used for its dehydrating and diuretic action. The deep injection method of administration eliminates the danger of acute respiratory paralysis, and permits a more sustained action.

3. Magnesium sulphate by mouth has a dehydrating action, by producing copious watery stools.

4. Fluids are forced because clinically this procedure seems to be helpful. Originally it was done with the idea of "washing out" the "toxin" from the blood, and encouraging diuresis. Theoretical support for this type of treatment has been advanced recently by Lashmet and Newburgh<sup>12</sup> and Lashmet,<sup>13</sup> in dealing with patients with nephritic damage. The reasoning is that solids require water for their excretion through the kidney. If the amount of solid to be excreted is increased, then more water must be excreted. If this water is not supplied by ingested fluids, then fluids must be withdrawn from the tissues for this purpose. But the tissues in the eclamptic patient have become hydrophilic (Zangemeister<sup>15</sup>), possibly because of the retention of nonprotein nitrogen compounds (as suggested by Plass<sup>14</sup>), and do not give up their

fluids. Therefore if fluid is neither ingested nor freed from the tissues, the solids are retained, since they cannot be excreted. This chain of events is overcome by forcing fluids.

Hypodermoclysis is not used in the convulsive stage because of the danger of injury to the patient by the fixed needle. Relatively small amounts of hypertonic glucose are given intravenously. Large amounts are not used because of the danger of throwing a sudden strain upon the heart.

(5) Alkalies are administered for their diuretic effect and their power to decrease acidosis. They are also useful in combating infection, to which eclamptic patients are unusually susceptible. In general they are used "... for changing the 'milieu' of the organism" (Hofbauer).

6. The low protein diet is carried over from the treatment of nephritis. Its value is being questioned by many authorities, but until this type of diet is proved actually harmful, continuation of its use is justified on clinical grounds alone.

7. Sedatives are not used in the control of the convulsions, and only rarely are they needed for the restlessness which sometimes follows the convulsive stage. The patient "knocked out" with sedatives cannot drink fluids, which we are very anxious for her to do. The comatose patient needs no sedatives; indeed, her vital functions are already at a dangerously low ebb. The patient under sedatives may slip over into coma without warning, and thus deprive the attendant of this warning of the need of more drastic treatment. Finally, the patient in labor should not receive large doses of sedatives because of the danger of asphyxiating the newborn.

8. Most authorities agree that the labor and delivery should be conducted along conservative lines.

#### COMMENT ON THE EFFECTS OF VERATRONE

The effect of the hypodermic injection of a therapeutic dose of veratrone is startling, and may cause undue alarm to those unused to seeing it. The blood pressure falls rapidly, sometimes going as low as 50 systolic. This marked fall is transitory, but is followed by a more or less prolonged period during which the pressure is well below the original level. The heartbeat is slowed to 40 per minute in some patients, but soon picks up, and remains at 60 to 80 until the effect of the drug has worn off. The pulse rate usually follows the blood pressure level fairly closely. Atropine or morphine or both are antidotes for *veratrum viride*; neither was needed in this series.

Vomiting is an early effect. The vomitus is copious and usually green or black, possibly indicating the excretion of toxic materials from the liver. The degree of vomiting varies with the individual susceptibility of the patient.

The respiration is always slowed considerably, but never to such a degree as to be harmful.

It should be emphasized that the individual susceptibility to the drug is very marked. For this reason, the treatment cannot be absolutely standardized. The size and number of doses can be gauged only by the reaction of the patient to it.

#### RESULTS

There are 121 consecutive cases of eclampsia in this series. The relation of convulsions to labor was as follows:

Prepartum	43
Intrapartum	17
Pre- and intrapartum	3
Intra- and postpartum	2
Pre- and postpartum	3
Pre-, intra-, and postpartum	3
Postpartum	50
	<hr/> 121

Convulsions occurred before delivery in seventy-one cases, or in 58.7 per cent of the cases in this series. Of the fifty postpartum cases, twenty-three delivered and had convulsions before admission.

The total number of maternal deaths in this series is twelve, or 9.92 per cent. A brief résumé of the deaths is as follows:

CASE 1.—Admitted in coma following several convulsions. Convulsions controlled. Delivered spontaneously a macerated six-month fetus. Died twelve days postpartum. Necropsy showed acute purulent endometritis, infarct of the upper lobe of the right lung, and miliary abscesses of the right kidney.

CASE 2.—Admitted in coma following many convulsions. Examination of chest showed lobar pneumonia. Spinal fluid bloody, and under increased pressure. Died twenty-seven hours after admission. Necropsy not done. No convulsions after treatment was started.

CASE 3.—Admitted in coma following many convulsions. No convulsions in the hospital. Regained consciousness, went into labor spontaneously, but died on the way to the delivery room. Necropsy showed marked necrosis of the liver.

CASE 4.—Admitted in coma, eighteen hours postpartum, after repeated convulsions. Blood pressure 90/60. Died five and one-half hours after admission, of pulmonary edema and cardiac failure. Necropsy showed bronchopneumonia and pulmonary edema.

CASE 5.—Admitted semicomatose. Delivered spontaneously in ten hours. Developed convulsions seventy hours postpartum, had three, and died sixteen hours later. Necropsy showed bilateral cerebral hemorrhages, and fatty degeneration of the liver, with multiple subcapsular hemorrhages.

CASE 6.—Admitted in coma after many convulsions. Died twenty minutes after admission. No necropsy allowed.

CASE 7.—Admitted in coma following eleven convulsions. Convulsions controlled promptly, patient regained consciousness, went into labor, and delivered spontaneously. Temperature of 102° two days postpartum with signs of bronchopneumonia. Died four days postpartum of acute cardiac failure and bronchopneumonia. No necropsy.

CASE 8.—Admitted three days postpartum following series of convulsions. In coma on admission. Had convulsions forty hours and six days after admission. Developed marked rigidity of the neck and severe urinary tract infection. Died nine days after admission. No necropsy.

CASE 9.—Admitted conscious, but severely toxic. No history of convulsions. Improved under treatment. Died in her first convulsion while Braun bag was being inserted. No necropsy.

CASE 10.—Admitted in coma following several convulsions. Responded well to treatment. Braun bag inserted. Had two convulsions during labor. Delivered spontaneously, but immediately went into coma, and died twenty hours later. No necropsy.

CASE 11.—Admitted in coma following six convulsions. Convulsions controlled after one immediately on admission. Died of acute pulmonary edema twelve hours after admission. No necropsy.

CASE 12.—Admitted in coma following many convulsions. No convulsions in hospital. Flaccid paralysis of entire right side on admission. Spinal tap unsuccessful because of marked edema of back. Died in coma sixty hours after admission. No necropsy.

Case 6 received no antieclamptic medication. Of the 120 other patients in the series, 60 per cent had no convulsions after treatment was started, 15.8 per cent had only one convulsion, and 24.2 per cent had more than one convulsion after treatment was started.

There have been no deaths in the last fifty cases of eclampsia.\* We feel that better prenatal care and earlier hospitalization have played some part in this.

#### SUMMARY AND CONCLUSIONS

The treatment of eclampsia at the Cincinnati General Hospital is outlined.

Emphasis is placed upon the value of veratrum viride properly used. Proper use consists chiefly of individualization of dosage. The use is justified on theoretical grounds, and by the results obtained.

The results of the treatment are given. The gross mortality figure of 9.92 per cent in a series of 121 consecutive cases of eclampsia compares favorably with figures reported from clinics where other methods of treatment are used. No corrected mortality figure is given, because such a figure may be open to question.

The fact that no deaths have occurred among the last fifty patients in this series is explicable not only on the basis of careful treatment, but also on the basis of better prenatal care and earlier hospitalization in acute cases.

I wish to thank Dr. H. L. Woodward, my chief of staff, for his permission to review the cases presented above, and for his constructive criticism of this paper as a whole.

\*Since these figures were compiled we have treated six additional patients with eclampsia without a death, reducing the gross mortality rate to 9.45 per cent and increasing to 56 the series without a mortality.

## REFERENCES

- (1) *DeLee, Joseph B.*: The Principles and Practice of Obstetrics, ed. 6, Philadelphia, 1933, W. B. Saunders and Co., p. 396. (2) *Williams, J. Whitridge*: Obstetrics, ed. 6, New York, 1931, D. Appleton and Co., p. 669. (3) *Lazard, Edmond M.*: AM. J. OBST. & GYNEC. 26: 647, 1933. (4) *Fishberg, Arthur M.*: Hypertension and Nephritis, Philadelphia, 1930, Lea and Febiger, p. 179. (5) *Haselhorst, G., and Mylius, K.*: Zentralbl. f. Gynäk. 52: 1180, 1928. (6) *Hofbauer, J.*: Zentralbl. f. Gynäk. 42: 745, 1918. (7) *Hofbauer, J.*: AM. J. OBST. & GYNEC. 26: 311, 1933. (8) *Anselmino, Karl Julius, Hoffmann, Friedrich, and Kennedy, Walter P.*: Edinburgh Med. J. 39: 376, 1932. (9) *Cramer, Wm.*: J. Pharmacol. & Exper. Therap. 7: 63, 1915. (10) *Solis-Cohen, Solomon, and Githens, Thomas Stotesbury*: Pharmacotherapeutics, New York, 1928, D. Appleton and Co., p. 1321. (11) *Hare, H. A.*: A Textbook of Practical Therapeutics, ed. 20, Philadelphia, 1927, Lea and Febiger, p. 555. (12) *Lashmet, F. H., and Newburgh, L. H.*: J. Clin. Investigation 11: 1003, 1932. (13) *Lashmet, F. H.*: J. Mich. State Med. Soc. 32: 317, 1933. (14) *Plass, E. D.*: Bull. Johns Hopkins Hosp. 35: 345, 1924. (15) *Ibid.*: Referring to Zange-meister.

## A STUDY OF THE FETAL MORTALITY IN PATIENTS WITH ORGANIC HEART DISEASE

HAROLD M. TEEL, M.D., BOSTON, MASS.

(From the Department of Obstetrics, Harvard Medical School)

PROPER medical management of the cardiac patient during pregnancy involves great sacrifice of her time, curtailment of her activity, and a considerable expense, over and above that incident to pregnancy in the normal subject. The risk of pregnancy to her life is not negligible, even under optimum conditions. In the past, medical and obstetric discussion of the question whether or not a cardiac patient should undertake pregnancy has concerned itself almost wholly with the maternal risk, without due consideration of the baby. It would seem that the probability of obtaining a live baby should be an important factor in such a decision. An unusual opportunity for study of the fetal mortality associated with this complication is afforded by the large number of patients with heart disease who have been treated at the Boston Lying-in Hospital.

### 1. MATERIAL

A special heart clinic has been in operation for fifteen years at this institution under the direction of Dr. B. E. Hamilton.<sup>1, 2, 3</sup> During routine prenatal examinations all patients who present signs or symptoms which might be referable to heart disease are directed to this clinic for cardiac diagnosis. Those found to have organic heart disease are followed by the cardiologist throughout pregnancy, delivery, and puerperium. In addition to the patients from our own prenatal clinics, a large number of cardiac patients are referred to the heart clinic by the general hospitals of the community, by practitioners who do their own

relatively normal obstetrics, and by other obstetric institutions in which religious principles prohibit contraceptive advice, therapeutic abortion, and sterilization.

The material to be presented in this paper has been obtained from an analysis of all the cardiac patients cared for during the past ten years. The heart lesion has proved to be of rheumatic origin in over 90 per cent of the cases. No patient who had organic heart disease has been excluded. On the other hand, no patient has been included unless there were certain minimum clinical findings: such as (1) demonstrable cardiac enlargement, (2) persistent diastolic murmur, or (3) a major disorder of the beat, such as auricular fibrillation, flutter, or heart block. In doubtful cases free use has been made of the seven-foot x-ray plate, fluoroscope, and the electrocardiogram. All final diagnoses have been made by the consulting cardiologist.

## 2. GROSS FETAL MORTALITY FOR THE WHOLE GROUP

During the ten-year period of this study, 598 patients with organic heart disease have been treated and delivered in the hospital. Of this group, 514 were delivered after the twenty-eighth week, and the fates of these viable babies will be presented in detail. However, it would seem to be of considerable interest to present first the gross fetal loss for the whole group, including spontaneous and therapeutic abortions. This will be found in Table I.

TABLE I. GROSS FETAL MORTALITY FOR ALL CARDIAC PATIENTS IN THE GROUP

Total pregnant cardiacs in the series	598
Total babies	606*
Died undelivered	3
Abortions, spontaneous	14
Abortions, therapeutic	67
Total babies who reached viability	522
Babies discharged living and well	484
Stillbirths	15
Neonatal deaths	23
Gross fetal loss for the whole group	20.13%
Fetal mortality among viable babies (Born after twenty-eighth week)	7.28%

\*This figure includes abortions and 8 pairs of twins.

The gross fetal loss (20.13 per cent) is enlightening, and at first thought rather discouraging, although it should be pointed out that more than half of the babies lost were from spontaneous and therapeutic abortions. Abortions are not ordinarily included in computing fetal mortality. Nevertheless, this gross figure is of some importance, for it shows that without selection, cardiac patients have only an 80 per cent chance of having a baby that survives. However, if one excludes the relatively small group of cardiac patients with such severe damage that the risk of pregnancy to their own lives is excessive, it will be shown

later that the prospect of obtaining a living baby is excellent. On the basis of history and physical examination, it is possible before the onset of pregnancy to recognize a large majority of these patients with heart lesions which are too severe to allow them to carry the strain of pregnancy. This point has been emphasized by Hamilton. Such patients whose cardiac condition clearly contraindicated pregnancy made up the great majority in the group upon whom therapeutic abortions were performed, and a considerable proportion of those whose pregnancies were terminated because of failure while the baby was still premature.

3. FETAL MORTALITY FOR BABIES DELIVERED AFTER VIABILITY

There were a total of 514 patients in whom pregnancy terminated after the twenty-eighth week. In the cases of fifty-three it was necessary to deliver the patient prematurely because of the condition of the heart (usually because of the occurrence of congestive failure). In the others, either labor was spontaneous or elective cesarean section was done at term. The fetal mortality for these viable babies is presented with some detail in Table II.

TABLE II. FETAL MORTALITY FOR ALL VIABLE BABIES—IRRESPECTIVE OF METHOD OF DELIVERY OR CARDIAC CONDITION OF THE MOTHER AT DELIVERY

	DURATION OF PREGNANCY IN WEEKS AT DELIVERY		
	29 THROUGH 35 WEEKS	AFTER 35 WEEKS	TOTAL FOR GROUP
Total babies delivered	36	486	522
Discharged living	17	467	484
Stillborn	2	13	15
Neonatal deaths	17	6	23
Gross fetal mortality	52.77%	3.91%	7.28%

The mortality among the babies delivered after the thirty-fifth week (3.91 per cent) compares favorably with the general fetal mortality for the hospital (excluding prematures). Although the prematures made up less than 7 per cent of the whole group, they accounted for half of the loss of babies. As will be shown in the following section, the mortality in the premature group is unusually high.

4. FETAL MORTALITY IN THE PREMATURE GROUP

The total mortality among the premature babies of this group of cardiac mothers is considerably higher than that for prematures in general. Of the 36 viable babies delivered before the thirty-sixth week of gestation, only 17 survived. Of those lost, only 2 were stillborn, and 17 died subsequent to delivery. Thus, of 34 premature babies born alive, 50 per cent subsequently died. What are the factors which have contributed to this high neonatal death rate? It is not to be explained upon an undue proportion of very premature babies (at least so far as weight is concerned), for of the 17 babies who died, 12 weighed over 4 pounds,

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.



4 between 3 and 4 pounds, and only 1 weighed less than 3 pounds. Nearly all of the fatalities occurred within the first forty-eight hours. Death was usually preceded by cyanosis and labored respiration. At autopsy little was found except for atelectasis, evidence of the aspiration of amniotic fluid, and the sequelae of asphyxia.

The type of delivery seems to have been one important factor. In Table III is presented the fetal mortality for all babies whose birth weights were less than five pounds, related to the method of delivery.

TABLE III. COMPARISON OF THE FETAL MORTALITY IN BABIES UNDER FIVE POUNDS DELIVERED THROUGH THE PELVIS AND BY CESAREAN SECTION

	TYPE OF DELIVERY	
	PELVIC	CESAREAN
Babies discharged living	13	4
Neonatal deaths	2	11
Stillborn	0	0
Fetal mortality	13.33%	73.33%

Of the fifteen premature babies delivered through the pelvis, the mortality was only 13.33 per cent, whereas of a like number delivered by cesarean section, 73.33 per cent died. These findings for premature babies of cardiac mothers confirm those of Clifford.<sup>4</sup> In his studies of premature infant mortality he has shown that the neonatal death rate is much higher after cesarean than after any type of pelvic delivery, except for breech extraction. In his series of prematures of cardiac mothers, the neonatal mortality was 75 per cent for those delivered by cesarean, and 30 per cent for vertex presentations delivered normally or by low forceps.

The precise reasons why these prematures delivered by cesarean section have done so poorly are not entirely clear. However, several factors which would seem to bear some relation should be mentioned. First, as noted above, autopsies in the fatal cases show little other than atelectasis, evidence of aspiration of amniotic fluid, and the sequelae of asphyxia. Most of the cardiac patients delivered by cesarean section of premature babies were either in congestive failure at the time of delivery, or had been in failure, and had partially reestablished compensation. Thus, it is possible that many of these babies had suffered from mild asphyxia prior to, as well as during, delivery. Then, too, many of the patients were given morphine in preparation for operation. As has been shown by Clifford, the neonatal mortality of prematures whose mothers have been given morphine prior to delivery is very high. Another point may be mentioned, which may have some bearing on the asphyxial nature of the fetal cases. Many of these cesarean sections were done under local anesthesia, a procedure which necessitates gentle and somewhat slower operating than usual. The slight delay in the extraction of these babies from the uterus may have added in some degree

to a preexisting intrauterine asphyxia. A number have required resuscitation. Morphia is no longer used in the preparation of these patients for cesarean section. Indeed, it is preferred to give no medication whatever in preparing the mother of a premature baby for delivery by cesarean section. The operation is now done either under local anesthesia or with a minimum of drop ether.

Of the group of prematures delivered through the pelvis, only two mothers were in mild decompensation, and morphia was given in only one case. These facts undoubtedly help to explain the much lower fetal mortality in this group.

There is one other suggestion which may have some significance in the explanation of the very high neonatal death rate among the prematures delivered by cesarean section. Most of the babies in this group have been very well nourished. The mothers of the premature cesarean babies have usually been in bed for weeks or months before delivery, a circumstance which might tend to produce well-nourished infants. Possibly many of these babies have been more premature in weeks of gestation than the birth weights would indicate. One certainly sees the opposite condition fairly commonly in the thin premature baby of the toxemic patient, which, on the basis of weight alone, should be more premature than one would expect from the duration of pregnancy. Clifford states that these prematures of the toxemic patients, once they are born alive, have as good a chance for survival as any premature. His chart actually shows that the mortality among the prematures born alive of toxemic mothers is slightly less than that of similar babies born of presumably normal mothers, and much less than for those of any other group. Very likely this may be explained by the relatively greater maturity of the thin toxemic baby in actual weeks' duration of pregnancy, in comparison with its birth weight.

In Table III the conventional five pounds was used as the criterion of prematurity. Because it was suspected that the premature babies of cardiac patients (the activities of whom have been greatly restricted during pregnancy) might be somewhat heavier than other prematures on a basis of weeks' duration of pregnancy, the fetal mortality of all babies born of cardiac patients, regardless of the type of delivery, has been tabulated according to estimated weeks' duration of the pregnancy at the time of delivery. The result is seen in Table IV.

The result of the tabulation in Table IV is surprisingly consistent. For comparison, the same data are presented for the mortality of these babies on a basis of birth weight. This may be seen in Table V.

Comparing the two tables, it would appear that estimated weeks' duration of pregnancy is a more reliable index of the chance of survival than the actual birth weight. The former should be considerably more reliable than an *estimate* of the size of the baby in utero by palpation. For this reason it would appear that, at least when the duration of the

TABLE IV. NEONATAL DEATH RATE FOR ALL BABIES BORN ALIVE OF CARDIAC MOTHERS RELATED TO ESTIMATED DURATION OF PREGNANCY AT TIME OF DELIVERY

	ESTIMATED WEEKS' DURATION OF PREGNANCY AT DELIVERY				
	TO 32 WK.	33-34	35-36	37-38	39-40
Lived	4	8	20	73	372
Died	8	5	4	5	0
Per cent mortality	67	38	17	6	0

TABLE V. NEONATAL DEATH RATE FOR ALL VIABLE BABIES OF CARDIAC MOTHERS RELATED TO BIRTH WEIGHT

	BIRTH WEIGHT IN POUNDS				
	LESS THAN 3	3-4	4-5	5-6	6 plus
Lived	0	5	12	52	408
Died	2	4	8	5	2
Per cent mortality	100	44.4	40	8.77	0.49

pregnancy by dates has been consistent with obstetric examination, the likelihood of survival may be more accurately prognosticated on the basis of weeks' duration of pregnancy than by estimated weight of the baby. Whether the method of measuring the occipitofrontal diameter of the fetal head in utero by x-ray<sup>5</sup> will be of greater prognostic value remains to be seen. On the basis of the results shown in Table IV one may infer that the chance of survival is too small before the thirty-fifth week if the baby is to be seriously considered; the chance is reasonably good in the thirty-fifth and thirty-sixth weeks; and after the thirty-sixth week the chance of survival is excellent.

#### 5. THE RELATION OF TYPE OF DELIVERY TO THE FETAL MORTALITY OF MATURE BABIES

There were 462 patients delivered either after the spontaneous onset of labor, or by elective cesarean section at term. The various types of delivery and the fetal mortality of each are shown in Table VI.

TABLE VI. THE FETAL MORTALITY AFTER THE VARIOUS TYPES OF DELIVERY

TYPE OF DELIVERY	TOTAL BABIES DELIVERED	DIS- CHARGED WELL	STILL- BORN	DIED	PER CENT MORTALITY
Normal	179	168	9	2	6.15
Forceps (24 midforceps)	210	208	2	0	0.95
Breech extraction, version	24	21	1	2	12.50
Cesarean at term	57	56	1*	0	1.75

\*This stillborn baby was known to be dead before the operation which was done for abruptio placentae. Thus, the corrected fetal mortality for cesarean section at term for this series was nil.

It will be seen from Table VI that the gross fetal mortality following normal delivery is over six times that following forceps. This does not present the case for normal delivery quite fairly, since there were among the nine stillbirths delivered normally five monsters and one

macerated fetus. However, the fetal mortality after forceps delivery of 0.95 per cent speaks strongly in favor of this method as a routine in all cases in which spontaneous delivery does not occur within a few minutes after full dilatation is reached. There is much to be said for low forceps delivery from the standpoint of the cardiac mother. The bulk of the strenuous physical exertion of labor is expended in the expulsive stage, after full dilatation has been reached. It would seem then that the use of low forceps to eliminate the exertion incident to the second stage of labor is a very reasonable precaution in patients with heart disease. Forceps delivery serves the best interests of both mother and baby.

In view of the high fetal mortality among premature babies delivered by cesarean section, it is somewhat reassuring to find that among 57 cesarean sections performed on cardiac patients at or near term, there was but one baby lost. This baby was known to be dead before the operation which was performed because of premature separation of the placenta. Excluding this one case, there were 56 consecutive cesarean sections at term without a fetal death.

#### 6. THE INFLUENCE OF DECOMPENSATION AT THE TIME OF DELIVERY UPON FETAL MORTALITY

It has been found by Clifford that the highest mortality among premature babies is in that group delivered of decompensated cardiacs by cesarean section. He found that the mortality rate in a small series of such babies was about 80 per cent. In this study, a patient was not considered to be decompensated unless she had at least persistent râles at the lung bases. The fetal mortality according to type of delivery and duration of pregnancy at the time of delivery is given for the failure and nonfailure groups in Table VII.

TABLE VII. THE INFLUENCE OF FAILURE IN CARDIACS AT THE TIME OF DELIVERY ON THE FATE OF THE BABY

	DELIVERED FROM 29 THROUGH 35 WEEKS		DELIVERED AFTER 35 WEEKS	
	IN FAILURE	NO FAILURE	IN FAILURE	NO FAILURE
<i>Pelvic Deliveries:</i>				
Babies discharged alive and well	2	11	21	355
Babies died	0	3	1	0
Babies stillborn	0	2	3	8
Total	2	16	25	363
Fetal mortality	0	31%	16%	2.20%
<i>Cesarean Deliveries:</i>				
Babies discharged alive and well	1	3	20	64
Babies died	7	7	0	4
Babies stillborn	0	0	0	2
Total	8	10	20	70
Fetal mortality	87.5%	70.0%	0%	8.57%

The mortality of 87.5 per cent in this series for prematures delivered of cardiac patients in failure by cesarean section confirms the findings of Clifford. However, the fetal mortality after pelvic delivery of mothers in failure was not so great as might have been anticipated. Strangely enough, there were twenty babies who were delivered after the onset of the thirty-sixth week by cesarean section of mothers in congestive failure. All of them survived. It should be mentioned that most of the patients in severe failure were delivered by cesarean section, whereas in the group delivered through the pelvis the decompensation was usually mild. In the whole group of fifty-five patients delivered while in congestive failure, there were only five stillborn babies.

#### COMMENT

Study of the fetal mortality of this group of patients has brought out a number of points which parallel those already gleaned from investigations of the maternal risk in cardiac patients. The greatest fetal loss occurs in that rather small group of patients with severe heart lesions, most of whom, had they sought competent medical attention, could have been advised that their heart reserve was too low to withstand the strain of pregnancy. An unexpectedly large number of these cardiac patients who have had medical attention have either had no advice as regards the risk of pregnancy, or have failed to heed such advice. On the other hand, patients with well-compensated heart disease, without history of past failure or embarrassment, seem to tolerate pregnancy well under strict medical regime. For this large group of women the fetal mortality does not differ materially from that for normal subjects.

There will probably always remain a borderline group whose past histories reveal no failure and no gross loss of reserve, who will fail for the first time in the middle of pregnancy. Their babies are extremely important, for most of them will never subsequently be in as good condition to withstand the strain of pregnancy. These patients usually fail some time after the twentieth week. With a rare exception, they improve to a varying extent under bed rest and treatment. A few do so poorly that one is obliged to disregard the baby and interrupt pregnancy when improvement has become maximum. Another small group do so well that one may even send them home to be followed closely with instructions to lead a bed- and chair-life until near term.

Then there is that great middle class: patients whose condition improves sufficiently that one feels warranted in watching them from day to day under hospital conditions until the baby is viable. These patients present the greatest difficulty from the standpoint of fetal mortality. The problems are two: when has the baby a good chance for survival, and how shall the patient be delivered? As regards the viability of the baby, if the expected date of confinement is known with reason-

able certainty, it would appear that waiting until the thirty-sixth week, and if possible, the thirty-seventh, offers a more certain prognosis than estimation of the size of the baby. In these cases in which the mother is on the edge of failure, but not in severe or gross failure, there would appear to be little likelihood that the baby will succumb to asphyxia in utero. Of fifty-five patients delivered while in congestive failure, there were only five stillborn babies. The mothers of these babies were in severe failure. The choice of method of delivery is equally troublesome. As far as the baby alone is concerned, pelvic delivery which implies induction of labor is the method of choice. One hesitates to attempt the induction of labor on such a patient. Induced labors so far from term are often long and tiring and cardiac patients should not be subjected to such an ordeal. Rupture of the membranes is not infrequently ineffectual, and even bagging may fail. There are reports in the literature of artificial rupture of the membranes having been immediately followed by acute and fatal congestive failure in cardiac patients. On the other hand, in our past experience at least, cesarean section offers the poorest chance for the premature baby of the cardiac mother. Nevertheless, certainly for primiparas, and probably also for multiparas whose condition does not permit of awaiting term delivery, cesarean section will doubtless remain the method of choice. It would appear that premature babies do not tolerate well the moderate degree of asphyxia incident to the combination of impaired maternal circulation and cesarean delivery. The prognosis for babies born after the thirty-fifth week of pregnancy when the mother is on the edge of, or in, mild congestive failure is very much brighter. The high fetal mortality which has been experienced in the past in this premature group can probably be reduced considerably by getting all patients whose cardiac condition allows consideration of the baby into or beyond the thirty-sixth week. Quick removal of the baby under local anesthesia or after a minimum period of inhalation anesthesia without preliminary medication, especially without morphia, may also aid in reducing these premature deaths.

So far as the term babies of the compensated cardiacs are concerned, normal delivery, low forceps, and cesarean section all offer an excellent prognosis. In this series low forceps had the least mortality with only two stillborn babies and no neonatal deaths in 210 deliveries. In view of the fact that forceps delivery takes most of the strain from the second stage of labor, it is equally to be recommended from the standpoint of the mother.

#### REFERENCES

- (1) *Hamilton, B. E.*: Boston M. & S. J. 188: 987, 1923. (2) *Hamilton, B. E., and Kellogg, F. S.*: AM. J. OBST. & GYNEC. 13: 535, 1927. (3) *Hamilton, B. E., and Kellogg, F. S.*: Boston M. & S. J. 91: 1942, 1928. (4) *Clifford, S. H.*: J. Pediat. 5: 139, 1934. (5) *Clifford, S. H.*: J. A. M. A. 103: 1117, 1934.

## HEMORRHAGE IN LATE PREGNANCY\*

PHILIP H. SMITH, M.D., F.A.C.S., EVANSTON, ILL.

*(From the Department of Obstetrics and Gynecology, Evanston Hospital and the Northwestern University Medical School)*

UTERINE hemorrhage in the last trimester of pregnancy is one of the most formidable complications with which the obstetrician has to deal. It takes its place with infection and toxemia, to make up the three main causes of maternal death, while the fetal mortality approaches 50 per cent. Good results are very dependent upon a prompt diagnosis and correct treatment instituted as soon as the diagnosis is made.

It is our aim to individualize each case and employ that method which seems best fitted to the case, rather than routine procedures. Judgment and skill thus exercised are the factors which increase or decrease the mortality rate.

Bleeding in late pregnancy is of great significance and should be regarded as of the most serious nature until proved otherwise. Therefore we should hospitalize a bleeding patient at once, get her grouped for blood transfusion, and establish a diagnosis. If the baby has not reached viability and the bleeding is only slight, the treatment may be compromised in some cases and the patient watched in the hospital. She should never be allowed to go home before she is delivered. Listed in this report is the case of a woman who bled only slightly and after a brief stay in the hospital, went home, only to return in a few days bleeding profusely and with the cervix dilated. She was quickly delivered by version and extraction, the uterus packed and venoclysis given, but she succumbed one and one-half hours after admittance. Attention must be called to an observation recently made by Rueker:<sup>1</sup> "A woman with placenta previa rarely bleeds to death from her first hemorrhage."

A careful study has been made of the hemorrhage cases occurring in the Obstetrical Department of the Evanston Hospital over a period of ten years, in order to judge the results of our management of this complication.

The patients in the group presented include (A) those bleeding from a normally situated placenta which we term "premature separation." This is the "abruptio placentae" of DeLee,<sup>2</sup> and the "ablatio placentae" of Holmes;<sup>3</sup> and (B) those bleeding from a placenta situated near the cervical os, in the dilating portion of the uterus as palpated, or seen on examination: "placenta previa."

\*Read before the Chicago Gynecological Society, December 21, 1934.

This report does not include patients in whom bleeding resulted from trauma to the cervix, a placental separation during delivery, bleeding following vaginal examination, or late second stage bleeding, but only those in which a definite diagnosis could be made.

When a vaginal examination is necessary to establish a diagnosis or determine the state of the cervix, it is resorted to, but only after everything is in readiness for rupture of the membranes, insertion of a bag or version. There is no place in our plan of treatment for cervical packing or vaginal tamponade. The value of such a procedure is questionable; it requires time and is too likely to lead to infection. Kellogg<sup>1</sup> in a recent report of 437 cases speaks rather strongly against such practice. Rectal examination is also a dangerous practice if the case be one of placenta previa. Such an examination may start serious bleeding at a time when one is not able to cope with it.

During the ten-year period from January, 1924, to December, 1933, inclusive, there were 7,981 obstetric patients admitted to the Evanston Hospital, among whom hemorrhage was a complication in 95 cases, or one out of every 84 cases (1.2 per cent). Of these 95 cases, 35 were due to premature separation of the placenta, and 60 resulted from placenta previa. Thus, the incidence of premature separation was 0.43 per cent and of placenta previa was 0.75 per cent.

Before considering our treatment of these cases I wish to point out a number of factors or conditions which must be considered before the choice of procedure is made. If the case be one of placenta previa the following deserve much consideration: (1) Condition of the patient, blood loss, shock, etc.; (2) type of placenta previa; (3) state of the cervix; (4) parity and age; (5) period of gestation; (6) is the baby alive? (7) how many vaginal examinations? (8) are membranes ruptured and, if so, how long? (9) is the patient in labor and what is the progress?

Should the case be one of premature separation, two additional factors must be considered: *First*, the amount of placental separation and the state of damage to the uterine musculature. The extravasation of blood into the wall of the uterus might be sufficient indication for termination by cesarean section and the removal of the uterus, without which certain patients will bleed to death when delivered from below. This will occur because of the loss of the power of contraction and notwithstanding packing, ergot, and pituitrin. We have not, however, in this small series had to remove the uterus because of such a severe state of apoplexy. *Second*, the degree of toxemia, if any. It is easily appreciated that a very slight separation in a nontoxic patient might be treated expectantly, while the same amount of separation in a severely toxic patient would be treated entirely differently.



TABLE I. PLACENTA PREVIA

Cases of placenta previa	69
Primiparas	19
Multiparas	41
Average age of primiparas	29
Average age of multiparas	32
Placenta previa marginalis	45
Primiparas	14
Multiparas	31
Placenta previa lateralis	11
Primiparas	5
Multiparas	6
Placenta previa totalis	4
Primiparas	0
Multiparas	4

TABLE II. PLACENTA PREVIA. TREATMENT

Primiparas	19
Expectant	4
Artificial rupture of membranes	6
Insertion of bag	2
Braxton-Hicks version	0
Cesarean section	7
Low cervical	7
Classical	0
Blood transfusions	1
Multiparas	41
Expectant	3
Artificial rupture of membranes	9
Insertion of bag	18
Braxton-Hicks version	2
Cesarean section	9
Low cervical	4
Classical	5
Blood transfusions	4

TABLE III. PLACENTA PREVIA. RESULTS

Maternal deaths	2
Maternal mortality	3.3%
Total fetal deaths	20
(Including all babies dying in first two weeks)	
Fetal mortality	33.3%
Corrected fetal mortality	25.0%
(Excluding monsters and those below 7 months)	
Morbidity	21.6%

It will be noted in Table III that cesarean section was done in sixteen of the sixty cases of placenta previa, an incidence of 26.6 per cent. The cases terminated by this method were those of placenta previa totalis, and those with an uneffaced, rigid cervix with a living baby. At or near term the fetal mortality is reduced nearly 100 per cent when placenta previa is treated by cesarean section. Three of our section babies, however, were definitely premature and failed to survive. Because of the frequency of fetal monstrosities in placenta previa, which was first pointed out by Greenhill,<sup>4a</sup> one must, in the interest of the baby,

make every reasonable effort to rule it out before an abdominal section. Five of the sixteen sections were classical operations, although we have almost given up the classical section; twelve classical operations were done in 1924, but none were done in 1932, 1933, or 1934. We do not feel that placenta previa is a contraindication to the low operation. This view is held by Daily,<sup>5</sup> Greenhill<sup>6</sup> and DeLee,<sup>7</sup> while Siegel<sup>8</sup> on the other hand, reports 101 cases in which only one low cervical was done.

It is our practice, if a woman is admitted in labor with the bleeding controlled by the presenting part, to treat her expectantly and with supportive measures, artificially rupturing the membranes if they are intact. Often one finds on first examination a cervix which will very shortly permit delivery. If spontaneous delivery does not occur it can be accomplished by forceps or version. Podalic version and extraction was done eleven times and seven women were delivered with forceps.

We restrict employment of a bag to control the bleeding, chiefly to the marginal type of placenta previa and rarely use it in a primipara. In only two primiparas were bags used. Both these babies were lost.

Braxton-Hicks version was done in two cases. These were both multiparas with a marginal type of placenta previa and in the one case the viability of the baby was questionable, while in the second case the baby was small and there were no fetal heart tones. We believe it should be restricted to cases of this character.

In all cases delivered from below the placenta is manually removed if there is continued bleeding. This was done in nine of the cases reported. Uterine and vaginal packing was used in ten cases. The cervix and vagina are routinely inspected for tears and while the records make note of several cervical tears, there were no deep ones through the placental site or into the broad ligament—a condition resulting most often from manual dilatation or delivery through an undilated cervix.

Blood transfusions were done in five of the cases reported. Fluids under the skin and by venoclysis have been used in nearly all the patients. Gum acacia solution in readiness for immediate use is always on hand in the maternity. It is of great value in combating shock and temporarily raising the blood pressure. I feel sure it aided materially in saving the lives of two of my patients, both of whom were admitted in a severe state of shock. The solution was given intravenously, while a bag was being put in and arrangements for transfusion made.

The maternal mortality of two in sixty cases (3.3 per cent) includes a multipara readmitted to the hospital with moderate bleeding and the cervix dilated. She was immediately delivered by version and extraction, packed and fluids given and, while a donor was in readiness, she died before blood could be given. The second case was a para ii, at term, who, after bleeding slightly for three hours with the membranes

ruptured, had a bag inserted which controlled the bleeding. Shortly following its expulsion she was delivered by version and extraction and the uterus packed. The packing failed to control the bleeding and the patient died a short time after delivery.

The fetal mortality of 25 per cent (including babies dead on admission) in the sixty cases reported compares favorably with other recent reports.

The morbidity in the series is 21.6 per cent following the standard set by the American College of Surgeons and the British Medical Association.

TABLE IV. PREMATURE SEPARATION

Cases of separation	35
Primiparas	15
Multiparas	20
Average age of primiparas	28
Average age of multiparas	31
Cases of toxemia	6
History of injury	1
Number of total separation	0
External bleeding occurred	35
Fetal heart tones absent on admission or disappeared before delivery	16

TABLE V. PREMATURE SEPARATION. TREATMENT AND RESULTS

Expectant	13
Artificial rupture of membranes	10
Insertion of bag	4
Cesarean section	8
Low cervical	4
Classical	4
Blood transfusions	4
Removal of uterus	0
Maternal deaths	1
Maternal mortality	3% (0.0268)
Total fetal mortality	62%
Corrected fetal mortality	26%
(This includes cases where no F.H.T. were heard on admission. It excludes babies below seven months and one anatomical anomaly)	
Morbidity	14.3%

While this series of premature separation is small, several things of interest are noted: First, the low incidence of toxemia, six out of thirty-five cases; and second, that external bleeding occurred in all patients; and last, there was one patient who had the complication with two successive pregnancies—both were interrupted by cesarean section and in neither was a live baby obtained.

Our diagnosis in the mild cases was based upon the hemorrhage, tenderness and rigidity, occasionally a sudden change in the character of the labor. In a few instances it was not definitely made until placenta previa had been ruled out by vaginal examination. The diagnosis, when the separation was more extensive, was made on the classical findings

of severe pain, marked rigidity of the uterus, fetal asphyxia, shock and increasing anemia. The outcome in any case rests upon the early recognition of the separation, its extent, the damage to the uterine musculature and the method used in treating it.

In the consideration of the treatment, I should like to point out that no uniform plan has been followed. For the most part the mild cases were treated expectantly and the severe cases by abdominal section. We have tried to keep in mind that it is not wise to be influenced too much by the baby's welfare, because of the very high fetal mortality. Bartholomew<sup>9</sup> reports 83.5 per cent mortality, Davis and McGee<sup>10</sup> 59.7 per cent, Polak<sup>11</sup> 87.5 per cent, and Wilson<sup>12</sup> 92.5 per cent.

Nearly one-half of the patients of our series were treated expectantly, many because there was only a mild separation in the course of labor and others because labor began with the onset of the symptoms of separation and progress was normal, without signs of increasing separation or fetal distress. With a change in the character of the pains, more bleeding and fetal asphyxia, more active treatment is begun. If the cervix is dilated and the head engaged, forceps delivery is done; if the head is unengaged, version is done. Nine of these patients were thus delivered: four by version and extraction and five by forceps.

Cesarean section was done eight times. It is restricted chiefly to patients not in labor and in whom there is much bleeding, shock and uterine damage. With proper supportive measures of blood transfusions, fluids by vein, morphia, etc., we believe cesarean section offers the best hope in the interest of the mother.

The third stage has been treated much in the manner as the treatment described for placenta previa; the placenta being manually removed for continued bleeding, and uterine and vaginal packing used in those cases where bleeding was not controlled or where there was doubt as to the ability of the uterus to remain contracted.

The one death in the thirty patients with abruptio placentae resulted from a ruptured aneurysm of the splenic artery with retroperitoneal and intraabdominal hemorrhage. This woman had been delivered a short time before by vaginal hysterotomy for premature detachment of the placenta.

#### SUMMARY

This study suggests that a fair percentage of the hemorrhages in late pregnancy may be treated expectantly with success.

An early diagnosis, the combating of shock and anemia by fluids and blood transfusions together with immediate treatment is essential for good results.

While cesarean section is the best treatment in selected cases, it should not be advocated as routine treatment. The low cervical cesarean section is not contraindicated in either placenta previa or premature separation.

## REFERENCES

- (1) *Rucker, M. Pierce*: J. A. M. A. 96: 1567, 1931. (2) *DeLee, Joseph B.*: Principles and Practice of Obstetrics, ed. 5, Philadelphia, 1928, W. B. Saunders Company. (3) *Holmes, R. W.*: Am. J. Obst. 44: 753, 1901. (4) *Kellogg, Foster S.*: New Eng. J. Med. 209: 1201, 1933. (4a) *Greenhill, J. P.*: Surg. Gynec. Obst. 36: 227, 1923. (5) *Daily, Edwin F.*: Surg. Gynec. Obst. 59: 106, 1934. (6) *Greenhill, J. P.*: Surg. Gynec. Obst. 50: 113, 1930. (7) *DeLee, Joseph B.*: Principles and Practice of Obstetrics, ed. 5, Philadelphia, 1928, W. B. Saunders Company. (8) *Siegel, Isadore A.*: AM. J. OBST. & GYNEC. 27: 889, 1934. (9) *Bartholomew, R. A.*: Premature Separation of the Normally Implanted Placenta, AM. J. OBST. & GYNEC. 18: 818, 1929. (10) *Davis, M. E., and McGee, W. B.*: Surg. Gynec. Obst. 53: 768, 1931. (11) *Polak, J. O.*: AM. J. OBST. & GYNEC. 21: 218, 1931. (12) *Wilson, P.*: Surg. Gynec. Obst. 34: 57, 1922.

636 CHURCH STREET

## SOME PROBLEMS IN PREGNANCY AND DIABETES\*

### AN ANALYSIS OF 20 PREGNANCIES IN 17 PATIENTS AND A PRELIMINARY REPORT ON 238 COLLECTED CASES IN THE LITERATURE

DAVID W. KRAMER, M.D., PHILADELPHIA, PA.

(From the Medical and Obstetrical Departments, Jefferson Medical College)

THE problems involved in diabetes and pregnancy have been frequently discussed in the literature. Since the advent of insulin, there is a prevailing opinion that the dangers arising in a pregnant diabetic individual may be minimized. Some intimate that diabetes mellitus should not be considered a contraindication to pregnancy. This again raises the question, shall we or shall we not advise a diabetic individual to undertake the responsibility of having a child? It is with this object that the author presents some of the aspects of diabetes and pregnancy, reports a study of the results of twenty pregnancies in seventeen patients and also an analysis of 238 collected cases from the literature. A survey on a larger scale will be published later.

The difficulties presented in a diabetic patient with pregnancy may be explained by a combination of circumstances working against the patient. We have to consider the disturbances that pregnancy may exert upon the diabetes, and, on the other hand, the influences of the diabetes upon the mother and child.

#### EFFECTS OF PREGNANCY UPON DIABETES

Before discussing this, a word or two about the minor derangements of the carbohydrate metabolism in the pregnant nondiabetic patient. Here the presence of sugar in the urine is not unusual. It may be transient or the glycosuria may persist. A vast majority of these patients have a normal blood sugar. As a rule the glycosuria disappears

\*Read, by invitation, at a meeting of the Obstetrical Society of Philadelphia, Nov. 1, 1934.

with the termination of the pregnancy. However, occasionally one meets with cases in which diabetes mellitus develops during the period of gestation.

Joslin<sup>1</sup> emphasizes the significance of glycosuria in pregnancy and the possibility of diabetes developing at this time. He recorded thirty-three such cases out of fifty-eight diabetics. These figures are rather high as diabetes complicating pregnancy is a rare occurrence. First,<sup>2</sup> in an examination of 1,000 consecutive records at the Jewish Maternity Hospital in Philadelphia, found only one case of diabetes developing during pregnancy. First,<sup>3</sup> in a survey of 5,000 pregnancies at the Preston Retreat in Philadelphia, reported only one case.

#### INFLUENCES OF PREGNANCY UPON ONE WHO IS ALREADY DIABETIC

Here the opinion is decidedly divided. Some are convinced that the diabetic condition may improve. On the other hand, while it is true that there may be an improvement of the tolerance during certain months of the pregnancy, there may be a decided lowered tolerance for starches necessitating increased insulin dosage, in other stages of gestation. This dissimilarity of views likewise exists in the period after pregnancy.

The improvement of the diabetes is attributed by many to the added secretion from the fetal pancreas. In favor of this argument are the works of Carlson<sup>4</sup> and others who noticed hyperplastic changes of the islands of Langerhans, both in animals as well as in the human fetal pancreas. Against this view is the fact that this does not exist in all cases. Ambard<sup>5</sup> and Morrison<sup>6</sup> have found fibrotic changes in the pancreas in some cases, and there are occasional reports of a newborn child dying from diabetes. If the presence of fetal insulin were so essential to the mother, would we not expect to increase the dose of insulin to supplement for the lack of the fetal secretion after delivery? This is not borne out clinically. If anything, the mother must be carefully watched, and it may be necessary to diminish promptly the insulin dosage in order to avoid severe hypoglycemic reactions.

It is quite possible that the explanation for any improvement may be the result of closer observation and better cooperation on the part of the patient, particularly when insulin is administered. The possibility of the fetus utilizing some of the available carbohydrates may also be mentioned.

The behavior of the diabetes during pregnancy is shown in Table I. Of the 110 available records, 52 showed improvement, 32 were worse, and 26 were unchanged.

The future course of the diabetic condition cannot be definitely evaluated. In some cases which were observed, a mild form of diabetes, easily controlled by diet, subsequently required insulin. On the other hand, in some severe cases the diabetic condition may be unaltered, even after trying experiences during the pregnancy and labor. However, one can-

not attribute the progress of the disease to the pregnancy. It may be due to neglect or failure to adhere to the diet.

*Coma* may come on suddenly with little warning. It was encountered in two of our series of twenty pregnancies (10 per cent). There were eleven cases reported in the collected series.

TABLE 1. STATISTICS OF 238 PREGNANCIES

	AUTHOR		SKIPPER		COLLECTED		TOTAL	
	CASES	%	CASES	%	CASES	%	CASES	%
Improved	5	25	4	10	43	24	52	21
Worse	9	45	11	29	12	6	32	13
Same	3	15	10	27	13	7	26	11
Not mentioned	3		12		113		128	
No. cases reported	20		37		181		238	

*Acidosis* is probably far more common than is generally supposed. It may exist with few or no symptoms and may explain some of the cases of coma that are precipitated with no apparent cause. An illustration of this fact may be gleaned from a record of a young severe diabetic who suddenly developed coma in the eighth month of her pregnancy. Two years later, while in the hospital for routine study during her second pregnancy, a severe acidosis was discovered with the  $\text{CO}_2$  as low as 28. There were absolutely no symptoms nor was there any discomfort. The acidosis was vigorously treated and the  $\text{CO}_2$  raised to 42. She subsequently was delivered of a live child.

*Effects of diabetes upon the pregnancy* may be manifested in the mother and in the child. Complications may appear in the form of miscarriages, abortions, therapeutic abortions, the necessity for induction of labor before term and hydramnios. Manifestations in the child will be discussed separately.

Miscarriage or abortions may result from the acidosis or may be due to some change, not clearly understood, in the reproductive organs that often exists in the diabetic patient. This statement is based on the well-known fact that there may be menstrual disturbances in the young diabetic and sterility is not at all uncommon.

There were five abortions, including two therapeutic abortions, out of twenty pregnancies (25 per cent) in our series. Skipper<sup>7</sup> reported twelve abortions, two of which were therapeutic, in a series of thirty-seven pregnancies (32 per cent), while Joslin mentioned thirteen in his series of eighty-nine pregnancies (14 per cent). *Induction of labor* may be necessary in the later months of pregnancy if the diabetic acidosis becomes extreme or if there is coma which cannot be controlled by insulin. This procedure may be necessary to save the life of the mother.

Induction may also be performed in an attempt to deliver a live child, especially if there is a history of a stillborn child in previous pregnancies.

*Hydramnios:* Regardless of the nature of this fluid, whether it be a secretion of the amniotic membrane or a urinary excretion from the fetus, it is an accepted fact that an excessive amount of amniotic fluid is not infrequent in diabetics. Skipper found an incidence of 27 per cent, but since the use of insulin, these figures have been reduced to 11 per cent.

*Hypoglycemic Reactions:* Hypoglycemic shock should also be kept in mind as this may endanger both the life of the mother and the child. Some feel that occasionally it may be responsible for fetal death. It also may jeopardize the life of the mother, particularly when there is danger of the condition's being unrecognized and mistaken for diabetic coma and treated accordingly. The added insulin may prove fatal.

*Effect Upon Delivery.*—Although various possibilities have been mentioned above whereby labor may be precipitated and pregnancy disturbed, we may say that in patients who have been carried along successfully to term by skillful management, the delivery need not be any more complicated than one may expect in nondiabetic patients. The danger of infection is not necessarily increased. The only possible difference may be a somewhat prolonged labor due to an overweight child.

*Effect of diabetes upon the child* is more or less interwoven with the effects upon the mother. Fetal mortality should embrace miscarriages, abortions, therapeutic abortions, and stillbirths, and some insist that deaths occurring within one to three days after delivery should be included. The high death rate is due to various causes, most important of which are acidosis and coma, hypoglycemic reactions, an overweight fetus, possible changes in the reproductive organs which may account for some of the miscarriages early in the pregnancy, and occasionally to diabetes itself.

Statistics show that the death rate of the child ranges from 37 to 65 per cent, the collective figures showing an average of 43 per cent. The largest group comes under the heading of stillbirths, which deserves some comment.

*Stillbirths:* The incidence of stillbirths in diabetics varies. In our records there were sixty stillbirths out of 238 pregnancies (25 per cent). The exact cause of death is not clear. Acidosis is the most likely explanation. However, there may be other contributory factors, either toxic, metabolic, or endocrine. It is presumed that carelessness upon the part of the patient and failure to carry out the diet rigidly are responsible for this unfortunate condition. In some cases, stillbirths occur despite the cooperation of the patient and skillful medical care.

The fetus evidently dies late in the course of the pregnancy. Fetal heart sounds may be heard until the second or third week prior to the expected time of birth. *Hypoglycemic shock* in the newborn must be kept in mind. The hyperplasia of the islands of Langerhans seen in



some cases may be instrumental in producing hypoglycemic reactions after birth, unless the child is given carbohydrates. This may explain some of the deaths occurring shortly after delivery.

*Overdevelopment:* An overweight child is frequently found in diabetes. This is so prevalent that even in nondiabetics the birth of an overgrown child suggests an investigation of the carbohydrate metabolism of the mother. This overdevelopment of the fetus is most likely due to the hyperglycemia of the mother. It is also possible that the normal pituitary function may be influenced in some way, thereby bringing about an increased skeletal development. The significance of an overweight child is obvious. It makes labor more difficult and prolonged, thereby increasing the liability to trauma during birth.

*Congenital Diabetes:* A hereditary tendency to diabetes is said to occur in from 16 to 35 per cent of the children. One may assume that this influence would be noticeable in the newborn child. Fortunately, this does not exist, as only two or three cases have been reported in which diabetes was discovered at birth or a few days after delivery. White<sup>6</sup> found only one case in 150 pregnancies of diabetic women in which the child developed diabetes at the age of five years.

*Prognosis.*—We will confine ourselves to the mortality statistics pertaining to mother and child.

In the author's series of twenty pregnancies, there were no deaths during pregnancy; two died within a year after birth. In a collected group of 238 pregnancies gathered from the literature, there were eight maternal deaths during pregnancy and the puerperium, seven died within one year and nineteen more up to three years, giving a total mortality rate of 14.2 per cent. This is practically in accord with Skipper's figures of 12.7 per cent in a collected series of 118 cases. A comparison of these figures based on the rate per 1,000 total births, with statistics<sup>9, 10, 11</sup> in nondiabetics is arranged in Table II. The significance of these figures is obvious. Comparing the diabetic mortality with the general puerperal death rate, the liability was about six times greater when we consider only the group of diabetic deaths occurring during

TABLE II. SHOWING MATERNAL DEATHS IN 238 PREGNANCIES COMPARED WITH AVERAGE PUERPERAL DEATH RATE IN PHILADELPHIA AND PENNSYLVANIA FROM 1929 TO 1933 (INCLUSIVE) AND THE CONTINENTAL UNITED STATES

	DIABETIC			PHILADELPHIA RATE PER 1,000	NONDIABETIC PENNSYLVANIA TOTAL BIRTHS	CON- TINENTAL UNITED STATES
	DEATHS	%	RATE PER 1,000			
During pregnancy	8	3.3	33	{ 5.1 ( 5 yr.) 6.39 (10 yr.)	5.7	6.46
Up to 1 year	7	2.9	29	----	--	---
1 to 3 years	19	7.9	79	----	--	---

pregnancy and the puerperium. The liability is even greater when we consider the total number of deaths up to the three-year period. The causes of death are usually diabetic coma or heart failure.

*Fetal Mortality:* There were 114 live births out of 238 pregnancies (47 per cent), equivalent to 470 in 1,000 total births. Compare these figures with the average of 95.7 per cent in Philadelphia and somewhat less than the 96 per cent in Pennsylvania (Table III). In the diabetic

TABLE III. SHOWING THE NUMBER OF LIVE BIRTHS AND STILLBORN IN DIABETICS COMPARED WITH THE AVERAGE LIVING BIRTHS AND STILLBORN IN PHILADELPHIA AND PENNSYLVANIA FROM 1929 TO 1933 (INCLUSIVE)

	DIABETIC		NONDIABETIC	
	NO.	PER CENT	PHILADELPHIA AVERAGE FROM 1929 TO 1933 INCL. PER CENT	PENNSYLVANIA PER CENT
Survived	114	47.0	95.7	96
Stillborn	51	21.0	4.2	4
Died within 3 days	14	5.8	---	--

group, one out of every five pregnancies may be a stillbirth, whereas only one in twenty-five occurs in nondiabetics. The diabetic liability is evidently five times greater than the ordinary pregnancy.

*Management of Diabetes and Pregnancy.*—The patient should be impressed with the necessity of cooperating faithfully, adhering to the diet and general care.

Frequent observations with routine urine and blood examinations should be made. Hyperglycemia should always be controlled.

The diet should be ample for the mother's needs, but it is important to avoid overweight, having in mind the tendency to bear an overdeveloped fetus.

In later months, hospitalization is advisable, even if only for two or three days, so as to make thorough studies for acidosis and to standardize insulin dosage. Acidosis may exist without apparent signs or symptoms.

Coma may be precipitated without warning. It should be treated vigorously with insulin and, if there is no prompt response, the advisability of emptying the uterus should be considered.

Induction of labor may be necessary in the late months of pregnancy if diabetic coma appears and is resistant to treatment. Labor may be induced before term in an attempt to deliver a live child when there is a history of previous stillbirths.

*Method of Delivery:* If the patient's condition is satisfactory, the natural delivery is preferable. There is no contraindication to a brief gas anesthesia if desired. Cesarean section has been advocated by some as the method of choice because it is a rapid means of delivery. It certainly is preferred when the patient requires assistance during labor. Spinal or gas anesthesia is far safer than ether or chloroform which have a tendency to induce or aggravate acidosis.

If laparotomy must be performed, the question of bringing about sterility should be kept in mind. This subject has been discussed by some writers in recent literature.

*Management of Postparturient Period:* Careful observation of insulin dosage and the blood sugar must be carried out. Hypoglycemic shock and coma are always possible developments and sometimes it is difficult, off hand, to differentiate between the two without proper blood studies.

When *lactation sets in, the blood sugar may drop and the dose of insulin must be diminished promptly.* This may be a temporary change. Later, the full dose of insulin may again be necessary.

Should the diabetic mother nurse her child? I do not see any objection to this, nor is there any danger if the mother's condition permits. However, I do think it will be to her advantage if the responsibility of breast feeding can be obviated.

The child should be carefully watched, especially for the first few days after birth, for the possibility of hypoglycemic shock.

#### SUMMARY AND CONCLUSIONS

The influence of pregnancy upon diabetes varies. There may be improvement at some period of gestation. Some attribute the increased tolerance to the added insulin secretion from the fetus. However, this explanation is more conjecture than one based upon scientific or clinical facts.

Acidosis may exist in the later months of pregnancy without symptoms or signs.

Coma is relatively infrequent but may develop suddenly in the late months of pregnancy.

Diabetes may influence the course of pregnancy by causing miscarriages, or abortions, necessitating therapeutic abortions or making induction of labor advisable before term to save the mother or the child.

Hydramnios is, relatively, a frequent occurrence in diabetes, ranging from a former percentage of 27 to 11 since the use of insulin.

The maternal death rate in diabetics is comparatively high. There were eight deaths during pregnancy and the puerperal period in 238 pregnancies. The equivalent rate per 1,000 total births would be 33.6 compared with the 5.7 in Pennsylvania and 6.46 in the Continental United States. If the rate included those who died within one to three years after birth, the figures would be comparatively higher, 79 per 1,000 births.

*Fetal Statistics:* There were 114 live births in 238 pregnancies (47 per cent) compared to 96 per cent live births in Pennsylvania in nondiabetics. Stillbirths are frequent occurrences in diabetics. There were fifty-one in the series of 238 pregnancies, or 21 per cent, compared to 4.2 per cent in Philadelphia statistics for nondiabetics.

The question as to *how we are to advise diabetics who desire children* cannot be answered without taking into consideration the condition of the patient and her ability to cooperate fully with the physician. The patient and family should be informed of the added risks, the likelihood of complications during pregnancy, plus the diminished chances of having a live child. However, there is always the possibility of going successfully to term if she is careful with her diet and if adequate insulin is administered. Treatment must be instituted early and maintained throughout the pregnancy.

The outlook for a mild or even moderately severe diabetic patient is fairly good provided the patient observes the rules. With the severe diabetic, the margin of safety is too narrow. Although these patients may go through the period of gestation without mishap, there is the constant danger of acidosis, and coma is always a menace.

In conclusion, the successful termination of pregnancy in a diabetic patient will depend upon the severity of the disease, frequent periodic examinations throughout the period of gestation, faithful adherence to the diabetic regime, and the skillful management of the case both by the obstetrician and the internist.

The author wishes to express his grateful acknowledgment to Drs. P. B. Bland, P. Williams, and J. Walker for their courtesies and privileges in observing patients on their services.

#### REFERENCES

- (1) *Joslin, E. P.*: Treatment of Diabetes Mellitus, Philadelphia, 1928, p. 869.
- (2) *First, A.*: Personal communication.
- (3) *Hirst, J. C.*: Personal communication.
- (4) *Carlson, A. J., and Ginsburg, H.*: Am. J. Physiol. 36: 217, 1915.
- (5) *Ambard, L. Merklcr, Schmid, F., and Wolff, M.*: Bull. et mém. Soc. méd. d. hôp. d. Paris 49: 547, 1925.
- (6) *Morrison, H.*: Boston M. & S. J. 175: 54, 1916.
- (7) *Skipper, E.*: Quart. J. Med. 2: 360, 1933.
- (8) *White, P.*: Diabetes in Childhood and Adolescence, Philadelphia, 1932, p. 42.
- (9) *Jones, E.*: Personal communication.
- (10) *Williams, P.*: Maternal Mortality in Philadelphia, 1934, p. 12.
- (11) *Murphy, T. F.*: Personal communication.

2007 PINE STREET

---

Steinert, J., and Papp, G.: Maternal Milk and Menstruation, Ztschr. f. Kinderh. 56: 208, 1934.

The investigations of Steinert and Papp in 30 nursing women revealed that the diastase content of their milk diminishes during menstruation. This decrease was greatest in women who had pronounced symptoms, notably headaches and anorexia, and whose nursing infants were markedly restless. The authors could not detect either hypophyseal or ovarian hormones in the milk.

J. P. GREENHILL.

## CANCER OF THE UTERUS IN CHILDHOOD

HAROLD A. LOCKHART, M.D., CEDAR RAPIDS, IOWA

CANCER in the early age groups is generally considered to be quite rare and, from a statistical point of view, this is true. Many of the signs and symptoms, which, if they occurred in an older person would arouse the suspicion of malignancy and lead to proper confirmatory or eliminatory diagnostic procedures, are explained by us as due to more common pathologic and functional entities.

Of the various childhood neoplasms, with the exception of those very obvious malignancies of the skin and the lymphangiomatous or hemangiomatous groups, those of the osseous system are probably less often missed. Giant cell tumors, intracranial neoplasms, as well as the bone sarcomas, by their early objective manifestations, are comparatively easy to diagnose. The hypernephroma, or as some prefer to call a probably closely related tumor now, the renal adenocarcinoma, with the symptoms of hematuria, and rapidly developing abdominal tumor, are not so long overlooked.

In this paper we are confining our remarks chiefly to neoplasms of the female genital tract, and particularly to the uterus.

D. H., was referred on June 19, 1932, at the age of two years and three months, with a complaint of vaginal bleeding and irritating vaginal discharge. She was first seen by a doctor on May 3, 1932, when fourteen months of age, and had had vaginal bleeding for two days. Smear at that time was negative, and she was put on argyrol instillations. When seen again on June 14, 1932, the bleeding had completely ceased, and a moderate discharge was present, which was again present on subsequent visits. Smears again were negative, and cleansing irrigations and instillations were advised. The mother then reported a recurrence of the vaginal bleeding on June 19, 1932. She was referred to us at that time.

The discharge had become foul in June, 1932, and remained so, increasing and decreasing throughout the twelve months. On June 18, there had been passage of bright red blood, with clots, from the vagina.

Family history was negative: three sisters and one brother all alive and well; no tuberculosis, syphilis, diabetes, malignancy, hemophilia, or other unusual tendencies in the family history.

Birth and development were normal until onset of present illness.

The child was well nourished and well developed. Genitalia externally were red-dened, with some hypertrophy of clitoris and labia majora; no adhesions. Urethra normal and hymen intact.

Probing of the vagina revealed no palpable foreign body, or undue resistance. Speculum examination in office not satisfactory. Rectal examination showed a rounded body, about the size of a small hen's egg, which gave the impression of being an enlarged uterus.

Smears were negative for gram-negative intra- or extracellular diplococci. A tentative diagnosis was made of either endometritis, endocervicitis (nonspecific), or perimetritis. Possibility of precocious menstruation. Warm boric acid douches were given, alternating with zinc sulphate and tannic acid.

She was next seen on July 1, 1933, discharge the same, with an exacerbation of the bleeding. Sleep good; bowels and bladder negative. No urinary disturbances.

On July 6, 1933, under ether anesthesia a bimanual rectoabdominal examination was done. The same sort of mass was outlined as before, but with more distinction; it seemed to be about apricot-sized, and involved the left half of the corpus and cervix uteri; was loosely attached anteriorly in the direction of the left horizontal pubic ramus; not fluctuant; but firm and fibrous. During, and after the examination, a few clots of dark blood escaped from the vagina.

A left mediolateral episiotomy, hymenotomy, and digital examination done: the mass seemed to be a part of the cervix, and invading the left fornix. Biopsy was taken from the anterior cervical lip, and also from a pedunculated mass of fibrous tissue in the left vaginal fornix.

Patient made good recovery from the operation and returned home.

*Pathologic Report.*—"Carcinoma," or, possibly, a "carcinosarcoma." After discussing the case with the parents, and roentgenologist, it was decided to give the



Fig. 1.

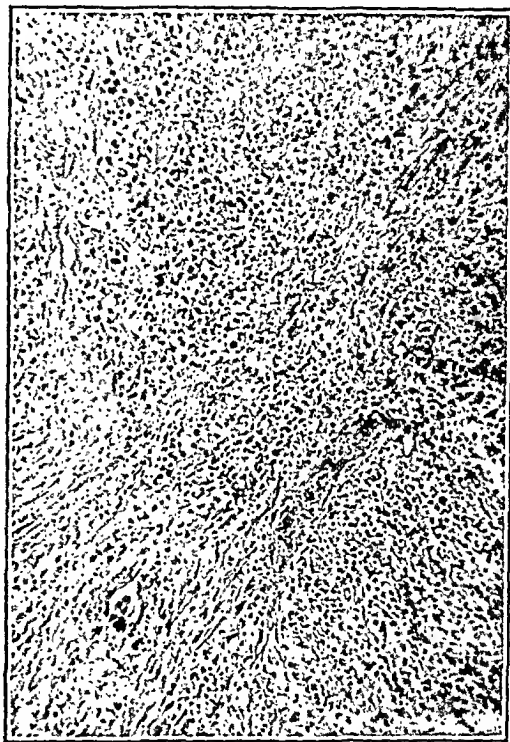


Fig. 2.

Fig. 1.—Shows a low power magnification of the infantile endometrium, with infiltration of carcinoma cells between the acini and down growth into the myometrium.

Fig. 2.—A low power view, showing widespread infiltration of the cancer cells into the myometrium; practically no acinar arrangement seen; many mitotic figures.

child a course of deep x-ray therapy, and if possible, extirpation of the mass might be considered later.

Between July 11, 1933, and Aug. 30, 1933, she was given a total irradiation of 1,100 roentgens, divided in six doses, three to the ventral part and three to the dorsal.

The patient was next seen on Sept. 23, 1933; she had been feeling good prior to this time, gaining weight. Recently she had been crying at night, and bleeding recurred on Sept. 22, 1933, passing about one ounce of bright blood from the vagina. Rectal examination revealed a definite decrease in size of the mass, which was now estimated at two-thirds of the original size, but still stony hard. It was

slightly more movable than on the previous examinations. The appetite was good; weight unchanged. Temperature 99.9°, axillary. She was given camphorated tincture of opium for pain.

On Oct. 21, 1933, urinary symptoms developed, with dysuria, retention, difficulty in starting stream, and passage of very small amounts frequently. Catheterization revealed a residual of 300 c.c. of dark, concentrated, cloudy urine (Sp. gr. 1.042). The child was passing quantities of blood each day, both from the vagina, and in the urine, and daily catheterization was done, with residual urine from 150 to 300 c.c. each time. One per cent mercurochrome was instilled into the bladder after washing it out with boric acid and normal saline solution.

From then on the course was rapidly downhill, with loss of weight and appetite, progressive anemia, and finally death on Nov. 3, 1933.

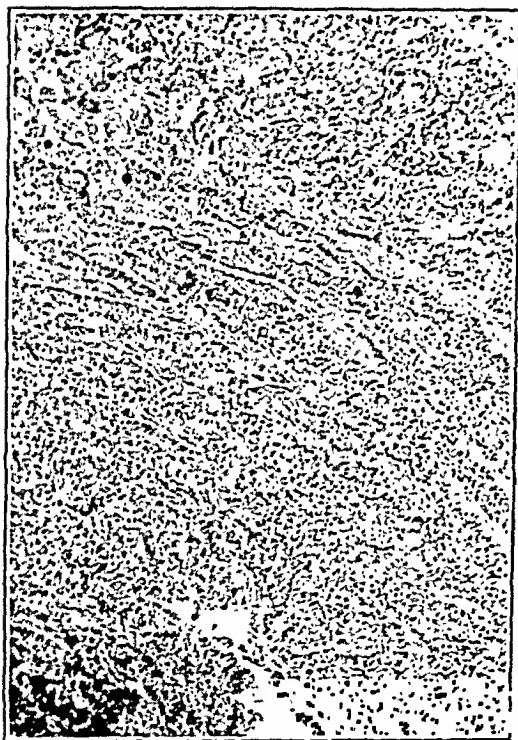


Fig. 3.



Fig. 4.

Fig. 3.—Low power showing invasion of malignant cells into muscle structure with little stroma and considerable attempts at glandular formation.

Fig. 4.—Section from papillary growth on the posterior wall of the urinary bladder.

*Necropsy Report.*—Liver was light colored, but no other evident changes; kidneys large, light colored, and showed moderate fetal lobulations. Marked cloudy swelling and moderate hydronephrosis. No evident changes in the spleen, pancreas, adrenals, and intestines. A few small tumor-like nodules in the lower part of the mesentery.

Urinary bladder: wall 4 to 6 mm. thick. There was a soft tumor mass on the anterior surface of the posterior wall, immediately above the trigone. This was 3.5 by 2.5 by 2 cm. thick. The tumor was spongy.

The uterus was 7 cm. long, 5 cm. broad; the wall was 2 cm. thick, and the cavity of the uterus was filled with black purulent fluid. There was considerable diffuse scarring and tumor growth in the wall.

Microscopic sections of the wall of the uterus showed the inner portion to consist of irregular masses of glandular epithelial cells. There was considerable diffuse

scarring of the wall of the uterus. Many of the epithelial cells of the mucosa were degenerated and necrotic. Very few were free from degeneration. The tumor cells of the bladder consisted of glandular epithelial cells occurring in tubules, and in papillary arrangement. There were a few mitotic figures in these cells. The small nodules in the mesentery consisted of lymph nodes containing small masses of glandular epithelial cells.

There was marked cloudy swelling and hydronephrosis of the kidneys. There were many small hemorrhages, and many round cells and leucocytes in the pelvic portion of the kidneys. The liver showed a moderate amount of fatty changes, and many round cells in the portal spaces.

*Anatomic Diagnosis.*—Carcinoma of the uterus, with extension to adjacent structures, and metastasis to mesentery, hypogastric, iliac, and inguinal nodes; acute and chronic cystitis; acute nephritis and hydronephrosis; fatty changes, and cloudy swelling of the liver.

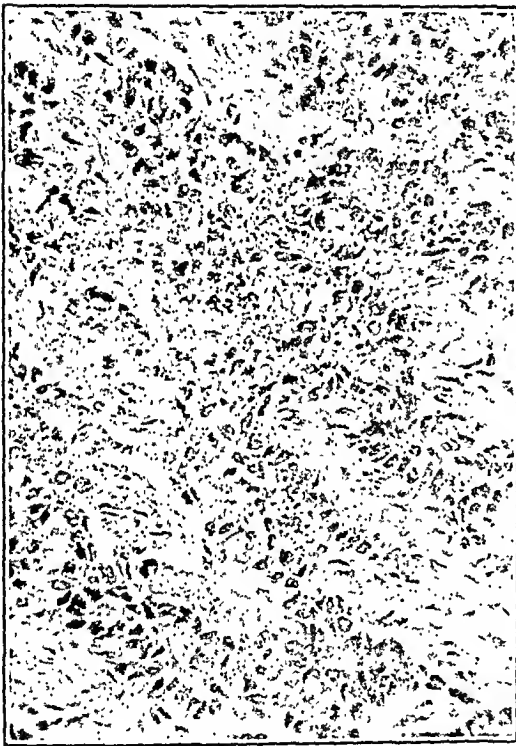


Fig. 5.



Fig. 6.

Figs. 5 and 6.—Oil immersion magnification of the malignant tissue in the uterine walls, showing many mitotic figures, much degeneration and necrosis seen.

During the last three weeks of life the mass became palpable abdominally, and extended about two fingerbreadths above the symphysis, and to the left of the mid-line. The weight loss was progressive, and the last weight, about one week before death, was 21½ pounds.

Dr. James Ewing of New York examined the sections and gives the following opinion: "an adenocarcinoma, papillary type, but with considerable infiltration of the wall of the uterus. The tumor has been rather bulky, and much of it is necrotic, but the outer portions are well preserved. The structure does not differ greatly from some endometrial carcinomas of adults. It is not distinctly embryonal, and therefore, I think it probably arose from the once normal infantile endometrium. It is, of course, quite malignant, but not more so than any of the adult adenocarcinomas of the uterus."



In the twelve cases of carcinoma of the uterus reported in the literature, besides the one of our own, as well as the other neoplasms of the uterus, one is struck by the frequent early fatal outcome. Usually the malignancy is inoperable when first seen, and nowhere near approaches the 50 per cent operability of all uterine carcinoma (cervical and corporal), such as was found in the carcinoma seen recently at the Mayo Clinic as reported by Mahle, and in some of the Berlin clinics, as noted by Semmelweiss.

The best results can be obtained, as in adults, by early diagnosis, careful investigation of suspicious cases, and the use of preliminary irradiation therapy, followed by appropriate surgery if possible. In the few cases where it is seen early, and localized to the cervix, radium, or even deep x-ray, may effect a complete cure, and this should be attempted prior to surgical attack.

---

## MERCUROCHROME TO SECURE VAGINAL ANTISEPSIS DURING LABOR

### A REPORT OF SIX THOUSAND CASES

H. W. MAYES, A.M., M.D., F.A.C.S., BROOKLYN, N. Y.

*(From the Obstetrical Department of the Methodist Episcopal Hospital)*

THE report of the Committee on Maternal Mortality in the City of New York has renewed the interest of the profession in the cause and prevention of puerperal deaths. According to that report, a large number of the deaths were charged to the physician, and of these, at least 40 per cent were ascribed to puerperal sepsis. If we would lower the mortality rate from childbirth, let us begin by reducing the number of deaths from infection. We can control deaths from toxemia and prevent deaths from postpartum hemorrhage in the majority of cases, providing the mother has had adequate prenatal care and proper precautions are taken. It is my belief that it is by the adoption of vaginal antisepsis that further progress must be made.

### CHOICE OF ANTISEPTICS

The ideal antiseptic to use for the disinfection of the birth canal should be powerful enough to destroy or inhibit the multiplication of the vaginal flora, noninjurious to the mucous membrane, and should not retard the healing of the lacerated tissue by any destructive action on the submucous structures. It should mix easily with blood and mucus and still retain its antiseptic qualities after dilution or concentration (by drying). Its repeated application should not cause discomfort to the patient, or reaction in the vaginal mucosa or skin of the perineum.

We have used a 4 per cent solution of mercurochrome for ten years and, although there may be some objection because of its staining

qualities, we feel that it has proved entirely satisfactory. We have had no reactions which have been injurious either to mother or child, and we are convinced that when the instillation is done before the cervix is fully dilated, and at least one hour before delivery, the vaginal flora is destroyed to such an extent that serious puerperal infection is almost impossible. The presence of the mercurochrome not only protects the patient from the bacteria already in the vagina, but also prevents infection from being introduced from other sources, during labor and delivery.

#### BACTERIOLOGY OF THE VAGINA

Much has been written on this subject during the last few years and only recently Douglas and Rhees<sup>1</sup> have reported on intranterine cultures taken during the postpartum period. A large number of organisms were found; 73.6 per cent were anaerobic streptococci, of which 8.1 per cent were facultative aerobes that might have played a rôle which would have caused a morbidity, or even a mortality, had not the protecting mechanisms of the mother been sufficient to withstand the invasion of the maternal tissues. Experience proves that these powers of resistance are not always present.

*Technic.*—The mercurochrome technic as we have used it at the Methodist Episcopal Hospital since Jan. 1, 1928, has been previously outlined in detail.<sup>2</sup> In brief, a 4 per cent aqueous mercurochrome solution is used to spray the perineum, except at the time of delivery, when a 4 per cent aqueous acetone solution is used. On admission of the patient, three drams of a 4 per cent aqueous solution of mercurochrome are instilled in the vagina by means of a special Asepto Vaginal Syringe, and this is repeated every twelve hours during labor.

The perineum and surrounding area can be prepared by any of several methods. The use of plenty of green soap and water should be satisfactory, and would undoubtedly destroy the majority of the bacteria. Iodine may be used, but it is irritating and its repetition may lead to a serious skin reaction which has proved troublesome and may itself be a source of infection. The repeated application of a 4 per cent solution of mercurochrome aids in keeping down the number of bacteria on the perineum and discourages infection from without. But this is not enough. *No matter how strong the antiseptic or how thorough the perineal preparation, some antiseptic must be instilled into the vagina in order that the preparation may be adequate and the entire responsibility of the doctor fulfilled.*

A few obstetricians report that they have used mercurochrome and have had no better results than without vaginal instillation. Success with the mercurochrome technic demands that it be properly carried out. *One instillation, even though an ounce of solution be used, is not sufficient if done immediately before delivery, rupturing membranes, or any operative interference.* It must be done at least one hour before any procedure is undertaken. The labia must be held firmly about the syringe in order that the solution may enter the vagina under some pressure.

An analysis of the morbidity of 6,285 cases delivered since Aug. 1, 1930, shows a gross morbidity, omitting the cesarean sections, of 5.5 per cent.

TABLE I. MORBIDITY REPORT FROM AUG. 1, 1930, TO JAN. 1, 1934

	CASES	MORBID- ITY	PER CENT MORBID- ITY	MORTALITY	
				TOTAL	VIA BLE VAGINAL DELIV- ERIES
Deliveries	6,285	474	7.5	13	
Cesarean sections	230	139	60.4	6	
Deliveries less cesarean sections	6,055	335	5.5	7	4
Ward	3,618	225	6.2	5	3
Private	2,437	110	4.5	2	1
Primiparas	2,968	198	6.6	1	
Multiparas	3,087	137	4.4	6	4
Spontaneous	3,418	166	4.8	2	2
Operative	2,637	169	6.4	5	2
Low and prophylactic forceps	2,118	119	5.1	1	1
Medium forceps	351	33	9.4		
High forceps	28	1	10.7		
Versions	48	5	10.4	1	1
Inductions	92	11	11.9	3	
Breech	310	16	5.1	1	1
Scanzoni	61	5	8.1		
Left occiput anterior	2,878	155	5.3	3	2
Right occiput anterior	1,470	85	5.7	1	1
Left occiput posterior	464	43	9.2		
Right occiput posterior	575	41	7.1	1	1
Lateral episiotomy	3,059	195	6.3	1	1
Median episiotomy	458	17	3.7		
Postpartum hemorrhage	145	34	23.4	3	2
Premature separation of placenta and accidental hemorrhage	82	17	20.7	1	
Anemia	54	20	37.03		
Placenta previa	56	17	30.3		
Eclampsia	28	6	21.4		
Toxemia	558	59	10.5	2	1

TABLE II. ETIOLOGY OF MORBIDITY FOR THE YEARS 1930-1934

Total deliveries less cesarean section		6,055
Morbidity		335 or 5.5%
Corrected morbidity		172 or 2.8%
<i>Due to Delivery</i>		
Lochometra	60	Reaction 6
Puerperal infection	8	Unclassified 24
Sapremia	34	No note 2
Endometritis	17	Examination negative 5
Parametritis	5	
Salpingitis	1	<i>Not Due to Delivery</i>
Phlebitis	1	Respiratory 24
Retained membranes	3	Breasts 66
Retained placenta	1	Pyelitis 68
Infected perineum	5	Tuberculosis 2
		Cystitis 3

Ninety-four cases had a morbidity of two or three days and have been classified as being due to either lochometra or sapremia. Whether this is correct, or whether these patients had a low-grade intrauterine infection which should have been classified as puerperal infection, is difficult to determine.

The corrected morbidity for the series was 2.8 per cent. In determining the corrected morbidity 163 cases were omitted, and of these respiratory, breast, and kidney infections accounted for 158. Some of these temperatures may have been due to other causes, but it is also true that many cases classified as due to delivery may belong to this group.

TABLE III. MATERNAL DEATHS, 1930-1934

Total deliveries	6,285
Total deaths	13
Cesarean sections	230
Cesarean section deaths	6
Deliveries less cesarean sections	6,055
Deaths less cesarean sections	7
Viable vaginal deliveries	4
Died undelivered or delivered before admission	1
Premature deaths	
From 3 to 7 months	2
Under 3 months	0
Died within 24 hours	2

A morbidity of short duration undoubtedly has little effect on the future well-being and convalescence of the mother, but when it is prolonged it is likely to cause damage which may lead to trouble in later years.

Of the six patients in this group, with morbid symptoms lasting twenty days or more, two were primiparas, one had a vaginal examination and her morbidity was due to a breast abscess. Only three patients were given an instillation during labor; one had a breast abscess, one a pyelitis, and the third had a temperature before delivery. Two of the six cases were operative and the morbidity was easily accounted for by conditions not due to delivery.

#### MATERNAL DEATHS

The death rate was 2.06 per one thousand deliveries while for the viable vaginal deliveries, it was a little over one per thousand. There were almost as many deaths from cesarean section as there were among the viable vaginal deliveries, and still the death rate was only 2.6 per cent.

TABLE IV. CAUSE OF DEATH

<i>Viable Vaginal Deliveries:</i>	7	<i>Cesarean Section Deaths:</i>	6
Breast abscess	1	Eclampsia	1
Cardiac case	1	Embolism	1
Necrosis of liver	1	Intestinal obstruction	1
Postpartum hemorrhage	1	Sepsis	1
Ruptured uterus	2	Toxemia	2
Toxemia	1		
<i>Delivered Before Admission and Not Delivered:</i>			1
Toxemia			1
<i>Between Three and Seven Months:</i>			2
Hyperemesis gravidarum			1
Ruptured uterus			1

There were no mothers lost from puerperal sepsis in this series of 6,055 viable vaginal deliveries, and if we were to include all such cases delivered since Jan. 1, 1928, there has been but one death in over 13,000 cases. This does not include a mother who died from embolism following an operation for breast abscess, nor does it include two women who had a normal temperature for two weeks, were discharged from the hospital, were later readmitted, and died from infection.

#### SUMMARY

The present mercurochrome technic at the Methodist Episcopal Hospital of Brooklyn, N. Y., was established Jan. 1, 1928, and since that time 11,564 patients have been delivered with a gross morbidity of

7.2 per cent and with 35 maternal deaths. Four hundred eight of these were cesarean sections, with a morbidity of 53 per cent and 11 deaths. There were 11,157 vaginal deliveries with a morbidity of 5.5 per cent, a corrected morbidity of 2.7 per cent, with 24 maternal deaths, in 11 of which cases the child was viable. During the experimental stages 5,253 patients were delivered, making a grand total of 16,817.

If we omit the cesarean sections, the following may be gleaned from the tables:

1. The ward morbidity was 6.2 per cent with 5 maternal deaths while among the private patients the morbidity was 4.5 per cent with 2 maternal deaths.

2. There was 2.2 per cent more morbidity among the primiparas than the multiparas, but 6 times as many deaths among the multiparas.

3. The morbidity of the operative cases was 1.6 per cent more than the spontaneous. If we consider only the viable vaginal deliveries, there was one death in 1,700 among the spontaneous while with the operative there was one in 1,300.

4. In the last 6,000 cases only one patient in 1,000 had a morbidity lasting twenty days. Of the six with a prolonged morbidity only three were given an instillation during labor, one of which had a breast abscess, one a pyelitis, and the other a temperature before delivery.

5. Loehiametra was given as the cause of morbidity in 60 cases and sapremia accounted for 34. In the causes of morbidity not due to delivery, respiratory conditions accounted for 24, mastitis 66, and pyelitis 68.

6. There have been 13,525 deliveries since the establishment of the present technic with 39 deaths, six or 15 per cent were due to puerperal sepsis, while there were only 14 deaths in 13,063 viable vaginal deliveries and only one of these was attributed to puerperal sepsis.

#### REFERENCES

(1) *Douglas and Rhces*: AM. J. OBST. & GYN. 27: 203, 1934. (2) *Mayes*: Surg. Gynec. Obst. 54: 529, 1932.

494 FIRST STREET

---

Sodano, Arcangelo: The Passage of Agglutinins Into the Maternal Milk, Arch. di ostet. e ginec. 20: 77, 1933.

Experimenting with the colon bacillus, Sodano found that the amount of agglutinins in the milk of the nursing mother was nearly as great as in her blood serum. In a group of patients who were immunized to the colon bacillus by vaccines during the latter part of pregnancy the milk was greatly inferior to the blood serum in agglutinin content, showing that the agglutinin content of the milk is not increased by increasing the blood serum content.

JAMES M. PIERCE.

## THE TREATMENT OF ELUSIVE ULCER OF THE BLADDER BY THE APPLICATION OF PURE PHENOL\*

NATHAN P. SEARS, PH.D., M.D., SYRACUSE, N. Y.

(From the Department of Clinical Gynecology, Syracuse University)

IN 1914 Hunner<sup>1</sup> described a lesion of the urinary bladder to which, because of the difficulty experienced in locating it, even when its existence was suspected, he applied the name "elusive ulcer." In 1921 Kretschmer<sup>2</sup> described his experience with this condition and called attention to the fact that Nitze<sup>3</sup> in 1907 had described a bladder ulcer identical with the one discovered by Hunner. Relatively infrequent, this lesion occurs often enough to be seen by the gynecologist three or four times yearly.

The most conspicuous symptom of this lesion is distress of long duration. The complaint of the patient is usually expressed as frequency of urination and burning during the act. Careful questioning will, however, frequently reveal the occurrence of a suprapubic pain when the bladder is full, and the occasional appearance of a small amount of blood in the urine when the patient has been forced to postpone emptying it. The burning and frequency may be due to complicating chronic urethritis and trigonitis, but suprapubic pain accompanying vesical distention directs attention to the possibility of "elusive ulcer." Intolerable frequency is an all important symptom.

A description of the histopathology of this ulcer has been carefully made by Hunner,<sup>1</sup> Kretschmer,<sup>2-4</sup> Frantz<sup>5</sup> and others. The lesion when seen by cystoscopic examination usually appears in the vertex or dome of the bladder. Keene<sup>6</sup> states that in none of his twenty patients was the trigone or ureteral area involved. The lesion is seen as a small, usually single superficial abraded area, which bleeds easily. Under good illumination one finds a pale, elevated, edematous area several centimeters in diameter surrounding this superficial ulceration. At one time or another the epithelium may be temporarily intact and the lesion easily overlooked. I have on occasion searched five or six times for an ulcer, the existence of which was suspected from the history.

One whose practice is limited to diseases of women has an advantage in the use of the Kelly cystoscope and the knee-chest posture. With this method one looks easily at the vertex or dome of the bladder through air. The sudden distention of the bladder through the Kelly instrument often causes the ulcer to bleed, and the trickle of blood traced to its source discloses it. If one suspects this lesion and sees the pale edematous area of thickened bladder wall, a stroke with a

---

\*Received for publication, January 18, 1935.

cotton applicator may produce bleeding and also cause the patient to exclaim with pain which she will identify as the one which has caused her to seek treatment. Using the end of the cystoscope as a measure, the exact size of the area may be determined.

Besides the cystoscopic findings, physical examination discloses little. The urine from patients with *uncomplicated* "elusive ulcer" shows only rare white and red blood cells. Vaginal examination may reveal tenderness of the bladder in the region of the ulcer. The occurrence of suprapubic pain, the chronicity of the lesion, the scarcity of abnormal elements in the urine and the difficulty in locating the lesion on cystoscopic examination has frequently led to unnecessary operations upon the abdominal and pelvic organs.

The treatment of this condition has not been satisfactory.

Hunner,<sup>1</sup> Kretschmer,<sup>2-4</sup> Frontz,<sup>5</sup> Keene,<sup>6</sup> and others for some time resected the ulcer-bearing wall of the bladder with rather unsatisfactory results. Recurrences were fairly frequent and in some instances a second operation was performed. Kretschmer<sup>7</sup> and Furniss<sup>8</sup> were among the first to report favorable results with the use of high frequency fulguration. This procedure is still used and will give long periods of relief. It usually requires, however, an anesthetic and promises no permanency of cure. I have seen two rather brisk hemorrhages eight to ten days after treatment. Bumpus<sup>9</sup> has had success with hydraulic distention under general anesthesia.

When ureteral stricture is present many of the cases are relieved by dilatation of the stricture, with or without the application of silver nitrate to the ulcer. Regardless of local treatment, *infection, either focal or any other portion of the urinary tract must be eliminated.* One must also keep in mind the fact that urethrotrigonitis is a frequent accompaniment of elusive ulcer and will be confusing in the treatment as well as in the diagnosis.

Since treatment of this condition has been, up to date, rather uncertain and unsatisfactory, I wish to call attention to a simple, painless and inexpensive method which has so far been very satisfactory. After noting the beneficial effect of pure carbolic acid on ulcerative cystitis remaining after the removal of a tuberculous kidney, I used this agent in treating an elusive ulcer. I have now had four such cases. The treatment is always carried out in the office and is as follows: Ten per cent cocaine is applied to the urethra for five minutes, the bladder is then emptied by catheter, the patient placed in correct knee-chest posture, the vaginal orifice opened to allow air to enter the vagina, and a Kelly cystoscope introduced into the bladder. By means of a head mirror and reflected light, the lesion is located and studied, and, after aspirating all urine from the bladder vertex, is thoroughly swabbed with pure phenol. If any of the solution touches the normal mucosa it is immediately neutralized by an applicator saturated with alcohol. After the ulcer is thoroughly painted, the patient remains in

the knee-chest posture, with the cystoscope in place, for a few seconds until the action of the phenol has taken place. As the cystoscope is withdrawn, if the trigone and urethra are inflamed, they are painted with 10 and 5 per cent silver nitrate respectively. The air is then allowed to escape and the patient to go about as usual. There is often some increased discomfort for a few days about which the patient should be warned. The lesion is then inspected in about two weeks and may or may not require more treatment. At first I was afraid that the pure phenol would cause a slough and I not only immediately applied alcohol but did not paint the entire area thoroughly. I soon discovered that thorough application produced no untoward effects.

#### CASE REPORT

CASE 1.—Mrs. G., aged fifty-four. First seen on Mar. 3, 1932, complained that for several years she had frequent, painful urination, and a dull burning sensation deep in the lower left side of the pelvis. For several weeks there had been blood in the urine. Complete cystoscopy revealed a slight stricture of the right ureter and urethrotrigonitis. A few erythrocytes were found in a catheterized specimen of urine. Treatment of the ureteral stricture and urethritis gave some relief, but the burning pain in the lower left side and attacks of hematuria continued. On May 26, 1933, an ulcer of the elusive type was discovered in the left lateral wall about 3 cm. from the left ureteral meatus. Several applications of silver nitrate gave some but very temporary relief. On July 31, 1933, pure phenol was applied to the ulcer. The patient when last seen Dec. 28, 1934, was well and had had no symptoms since the application of phenol seventeen months previously.

CASE 2.—Mrs. S., aged fifty-four, first seen Jan. 18, 1932, complained of frequent and burning urination for eight months. After complete examination a diagnosis of chronic urethritis and trigonitis was made. Dental examination revealed an apical abscess and three other "suspicious" teeth. The abscessed tooth was removed. The patient was treated for trigonitis with considerable improvement. On Oct. 26, 1932, an elusive ulcer was discovered. The application of 10 and 20 per cent silver nitrate on several occasions produced some improvement, but there were frequent recurrences. On July 12, 1933, pure phenol followed by alcohol was applied to the bleeding area of the ulcer. A thorough application of phenol was made to the lesion on May 29, 1934. Since then there has been no recurrence of the ulcer. There have been occasional attacks of urethritis, but the patient has not yet had the "suspicious" teeth treated.

CASE 3.—Miss B., aged forty-six, seen Mar. 20, 1934, had had bladder trouble for nine years. Five years ago, a local urologist suspected tuberculosis of the kidney and bladder. She then went to another city where the diagnosis of Hunner ulcer was made. Animal inoculation at that time was negative for tuberculosis. The ulcer was fulgurated and treated with silver nitrate. The patient remained symptom-free for four years. My examination showed the old ulcer which was red and bled easily. It was about 3 cm. in diameter and was in the left part of vertex. Catheterized urine revealed many erythrocytes and a few pus cells. Three applications of silver nitrate were of little benefit. On April 7 and 21, and May 5 and 19, phenol was thoroughly applied. The patient, last seen on Oct. 19, 1934, stated that she had had no symptoms of any kind since her phenol treatment in April. The ulcer was perfectly healed but the urine contained pus. Since her



previous visit I had learned that three animals inoculated by the local urologist five years ago were actually positive for tuberculosis. A specimen of urine, containing numerous pus cells, was sent for animal inoculation and was reported positive for tuberculosis on Dec. 6, 1934. This patient has a typical "elusive ulcer," which seems to be accompanied by renal tuberculosis. Hunner<sup>10</sup> has several times had the same experience, and has found no evidence of tuberculosis in the tissue of the excised ulcer. A letter has been sent asking this patient to return for further study.

CASE 4.—Mrs. B., aged fifty-two, seen Oct. 5, 1934, complained of pain in the lower abdomen with severe day and night frequency and burning of urination for five years. She had also noted a tender spot just above the pubis. Cystoscopic examination four years ago is said to have given negative findings. On Aug. 23, 1934, an hysterectomy for uterine fibroids was done and a urethral polyp was removed. This operation had no effect upon the pelvic pain. My examination revealed a tender bladder and a few red blood cells in the urine. Kelly cystoscope examination showed a definite elusive ulcer at the junction of left base and vertex, also chronic urethritis. The touching of the ulcer with an applicator reproduced the pain for which the patient had consulted me. Pure phenol was applied to the ulcer on October 10 and 26. Five per cent silver nitrate was applied to the urethra on these dates and on October 19. On November 30 the ulcer was healed and for the first time in five years the patient had no symptoms. Definitely infected tonsils are to be removed soon.

#### SUMMARY AND DISCUSSION

Four cases of elusive ulcer of the bladder are reported. Overcautious at first, I soon found that the thorough swabbing of the ulcer caused very little distress and no complications, and was followed by prompt and prolonged relief.

A letter to Dr. Hunner in August, 1933, brought the reply that he had not used this treatment but would do so. The following is a quotation from his letter of Sept. 27, 1934: "I have had eight or ten cases since you wrote me about this and I have had nothing before to compare with the immediate results. Of course I have not had more than six or eight months on any of them, not long enough to say how long the results are going to hold. I have had enough experience with it, however, to feel that it is going to be a tremendous addition for our therapy in this rather unsatisfactory line of work." Hunner's experience encouraged me to report my small group of cases.

#### REFERENCES

- (1) Hunner, Guy L.: Boston M. & S. J. 172: 660, 1915. (2) Kretschmer, Herman L.: J. A. M. A. 76: 990, 1921. (3) Nitze: Lehrbuch der Cystoskopie, 1907, p. 208. (4) Kretschmer, Herman L.: Surg. Gynec. Obst. 35: 759, 1922. (5) Frontz, William A.: South. M. J. 21: 899, 1928. (6) Keene, Floyd E.: AM. J. OBST. & GYNEC. 10: 380, 1925. (7) Kretschmer, Herman L.: J. A. M. A. 86: 739, 1926. (8) Furniss, H. D.: AM. J. OBST. & GYNEC. 7: 288, 1924. (9) Bumpus, H. C.: Med. Clinic N. A. 13: 1495, 1930. (10) Hunner, Guy L.: AM. J. OBST. & GYNEC. 24: 706, 1932.

## THE USE OF DILAUDID IN GYNECOLOGIC SURGERY

T. K. BROWN, B.S., M.S., M.D., AND H. L. KLEINE, B.S., M.D.,  
ST. LOUIS, MO.

(From the Washington University School of Medicine Department of Obstetrics and Gynecology, Barnes Hospital and the St. Louis Maternity Hospital)

WHILE there are several reports in the foreign literature on the use of dilaudid (*dihydromorphinone hydrochloride*) given alone or with other drugs to relieve pain, a critical examination of the American literature fails to reveal any report on the use of dilaudid and scopolamine in surgery. The publications which have appeared may serve as criteria for matters of dosage, safety, and to suggest the possibilities of dilaudid in relieving pain in many fields of medicine.

Alvarez<sup>1</sup> first used the drug in America for the amelioration of pain in inoperable carcinoma, reporting quite favorably on it in August, 1932. Since then, Ruch<sup>2</sup> has reported good results with a combination of dilaudid  $\frac{1}{32}$  gr. (0.002 gm.) and scopolamine  $\frac{1}{130}$  gr. (0.0005 gm.) in producing analgesia in obstetric cases. Jacobs<sup>3</sup> also found dilaudid, when used alone or with scopolamine, capable of inducing a satisfactory analgesia for labor, yet without prolonging it, or without an untoward influence on the child. Weum<sup>4</sup> called attention to the use of dilaudid given in conjunction with a barbiturate in labor, postpartum and postoperative, and commented favorably on the action of the rectal suppositories.

In order to ascertain a satisfactory method of using dilaudid and scopolamine for surgical cases, our study was directed toward the use of this combination in gynecologic surgery.

One of the first European reports in this field was that of Ellerau,<sup>5</sup> who reported favorably on the use of dilaudid and scopolamine given preoperatively. Later von Octtingen,<sup>6</sup> who studied a similar combination given to almost 500 patients requiring gynecologic surgery, found it to produce a most satisfactory analgesia in over one-third of his cases, while about 60 per cent of the total number were only disturbed at times during the course of minor operations. More recently, Jost,<sup>7</sup> in a comprehensive series of 1,514 cases, gave  $\frac{1}{32}$  gr. (0.002 gm.) of dilaudid and  $\frac{1}{200}$  gr. (0.0003 gm.) of scopolamine two hours, and again one hour before the operation. An hour before the first injection, 0.5 gm. of veronal was given. In over 95 per cent of these cases, minor operative procedures could be carried on without an additional narcotic, though in some cases, the sleep was not deep enough to wholly prevent any reaction. Grossmann<sup>8</sup> and others have reported on the use of dilaudid alone preoperatively.

In this paper, we are reporting the use of dilaudid in a series of 225 gynecologic cases, largely surgical. This series consists of 100 cases where dilaudid-hyoscine was used preoperatively, 160 cases where dilaudid alone was used postoperatively, and 65 cases in which dilaudid suppositories were used postoperatively.

In the table below are given the types of cases and the number of each type, where dilaudid was used preoperatively with hyoscine. Hyoscine has exactly the same pharmacologic action as scopolamine.

Curettage, biopsy or radium implant	22
Vaginal and cervical plastic	24
Vaginal plastic and laparotomy	8
Suspension operation	4
Adnexal operation	10
Hysterotomy and sterilization	2
Supravaginal hysterectomy	14
Complete hysterectomy	14
Vaginal hysterectomy	2
Total	100

In each case (except in the small series where spinal anesthesia was used), two injections of hyoscine of  $\frac{1}{130}$  gr. (0.0005 gm.) each were given, combined with varying amounts of dilaudid. The first injection, consisting of dilaudid and hyoscine, was given one hour and forty-five minutes before the operation. The second injection was given one hour before the operation and consisted of hyoscine alone or in combination with dilaudid. The only sedative given consisted of a small dose of a barbiturate the night before operation. Table I shows the amounts of dilaudid used in all the cases and also the types of anesthesia.

TABLE I

DOSAGE	PREOPERATIVE				POSTOPERATIVE		
	$\frac{1}{48}$ GR. DILAUDID 2 C.C. HYOSCINE	$\frac{1}{32}$ GR. DILAUDID 2 C.C. HYOSCINE	$\frac{1}{48}$ GR. DILAUDID 1 C.C. HYOSCINE	$\frac{1}{128}$ GR. DILAUDID 1 C.C. HYOSCINE	$\frac{1}{32}$ GR. DILAUDID 1 C.C. HYOSCINE	$\frac{1}{48}$ GR. DILAUDID	$\frac{1}{32}$ GR. DILAUDID SUPPOSITORIES
No. of Majors Anesthetic	10 Gas Ether	5 Gas Ether	32 Gas Ether	7 Spinal	5 -	139 -	38 -
Analgesia and Amnesia	Fair	Good	Good	Good	Fair	Good	Good
Respiratory Depression	No	Yes	No	No	No	No	No
No. of Minors Anesthetic	5 Gas 3 None 2	41 Gas 25 None 16	-	-	12 -	4 -	27 -
Analgesia and Amnesia	Good	Good	-	-	Good	Good	Good
Respiratory Depression	No	No	-	-	No	No	No

In a small series of five cases,  $\frac{1}{32}$  gr. (0.002 gm.) of dilaudid was used with the first injection of hyoscine and none with the second. This was discontinued, because in three out of the five cases there was such a marked respiratory depression before the anesthetic was started that the operation had to be delayed until the breathing had been stimulated with  $\text{CO}_2$  inhalations. Therefore,  $\frac{1}{48}$  gr. (0.0013 gm.) of

dilaudid was substituted for the  $\frac{1}{32}$  gr. No respiratory depression was noted. But in these analgesia and amnesia was not of sufficient depth except where the individual was small or senile. Therefore, the second injection of hyoscine was supplemented with an additional  $\frac{1}{128}$  gr. (0.00047 gm.) of dilaudid. Apparently then, the proper dosage for major cases had been found. Respirations were not depressed in this whole series. Nitrous oxide-oxygen-ether was used. Its induction was easy throughout, and slightly less was used than in a large control series using  $\frac{1}{6}$  gr. (0.01 gm.) morphine instead of dilaudid. Dilaudid was also used in a small series of cases followed by spinal anesthesia. In these, 1  $\frac{3}{4}$  gr. (0.12 gm.) of luminal was given the night before operation, 10 gr. (0.6 gm.) of sodium barbital one and one-half hours before the operation and one injection consisting of  $\frac{1}{32}$  gr. of dilaudid and  $\frac{1}{130}$  gr. of hyoscine one hour before the operation. The spinal anesthesia consisted of 3 gr. (0.2 gm.) of novocaine crystals dissolved in spinal fluid. Only in a few cases where the operation was unusually long was a small amount of gas-ether required.

In minor operations we found that  $\frac{1}{32}$  gr. of dilaudid given with the first injection of hyoscine and not repeated with the second was well tolerated as only gas or no additional anesthesia was used. If the individual was small or senile, we found that  $\frac{1}{48}$  gr. of dilaudid was sufficient. As can be seen from the table, almost half of the minor operations were carried out without any anesthesia. The results were uniformly as good as in the major operations.

There is indication of definite synergistic action between dilaudid and hyoscine. Care must, therefore, be exercised in the use of the larger dosage, especially when followed by deep surgical anesthesia, because of the danger of respiratory depression. It is apparently possible to obtain satisfactory analgesia and amnesia with reduced doses of hyoscine.

As to the analysis of individual cases, it was found that complete analgesia and amnesia were obtained in 83 per cent of the cases, moderately good in 15 per cent and poor in only 2 per cent. The action was more prompt with dilaudid than with morphine, the patient becoming drowsy five to eight minutes after the first injection. The amounts of inhalation anesthesia were definitely decreased and the patients reacted sooner after the operation.

In 160 cases, dilaudid alone was used postoperatively by means of hypodermic injection and in 65 cases by rectal suppository. Injections of  $\frac{1}{48}$  gr. doses were used in small or senile individuals or where the pain was only moderate. Doses of  $\frac{1}{32}$  gr. were used in the others.

Our results agree in the main with those of German investigators named above and others, including Siebner,<sup>9</sup> Sterchele,<sup>10</sup> and Seeliger.<sup>11</sup> Dilaudid relieved pain as well as, if not a little better than, morphine

and, of course, in much smaller doses. The action was more prompt with dilaudid and the mental faculties did not remain dulled as long afterward. Dilaudid did not depress the patient as much as morphine. The patient was clearer, more cooperative in her nursing care, and better able to feed herself and take fluids. Less inhibition of peristalsis with dilaudid than with morphine in laboratory tests has been reported. We found this to be true clinically, because there was definitely less distention when dilaudid was used in place of morphine. Less catharsis was employed and there were no cases of ileus in the entire series. Vomiting was definitely decreased. We also noticed that the number of postoperative catheterizations was slightly decreased when dilaudid was used.

The  $\frac{1}{24}$  gr. (0.0025 gm.) of dilaudid rectal suppository is a very easy and efficient way to administer the drug. Pain was relieved within fifteen to twenty minutes and for considerably longer periods of time than when given hypodermically. No untoward results were obtained. Since this series was completed we found the suppositories especially useful in the relief of pain in cases of advanced pelvic carcinoma.

#### CONCLUSIONS

1. Dilaudid may replace morphine in surgery.
2. It relieves pain and requires smaller doses.
3. There is evidence of synergism between dilaudid and hyoseine.
4. Dilaudid in larger doses, especially with hyoseine, causes respiratory depression.
5. The reaction and recovery from narcosis are more prompt with dilaudid.
6. There is less postoperative distention and less need of catharsis with dilaudid.
7. There is less vomiting with dilaudid.
8. Postoperative catheterization was required slightly less frequently with dilaudid.
9. Suppositories form an excellent means of administering dilaudid for a more prolonged action.

#### REFERENCES

- (1) *Alvarez, W. C.*: Proc. of the Staff Meetings of the Mayo Clinic 7: 480, 1932. (2) *Ruch, W. A.*: AM. J. OBST. & GYNEC. 27: 717, 1934. (3) *Jacobs, J. B.*: Med. Record, Mar. 21, 1934. (4) *Neum, T. W.*: Lancet 54: 713, 1934. (5) *Ellerau*: Klin. Wchnschr. 5: 2430, 1926. (6) *von Oettingen, W. F.*: München. med. Wchnschr. 74: 1184, 1927. (7) *Jost, F.*: Zentralbl. f. Gynäk. 58: 228, 1934. (8) *Grossmann, H.*: Med. Welt 2: 1823, 1928. (9) *Siebner, M.*: Fortschr. d. Ther. 7: 349, 1931. (10) *Sterchele, G.*: Pensiero Med. 16: 214, 1927. (11) *Secliger, P.*: Wien. klin. Wchnschr. 40: 495, 1927.

## ECTOPIC PREGNANCY

### THE RESULTS OF IMMEDIATE OPERATION AND THE VALUE OF SPINAL ANESTHESIA

HARRY KOSTER, M.D., F.A.C.S., AND WILLIAM I. SHEINFELD, M.D.,  
BROOKLYN, N. Y.

*(From the Crown Heights Hospital)*

IN THE five-year period from Jan. 1, 1929 to Jan 1, 1934 out of 6,581 laparotomies on a general surgical service, ectopic pregnancy was encountered sixty-nine times. These patients were all operated upon on one service by one operator who followed a routinized surgical procedure. They all received spinal anesthesia, no distinction being made between the so-called tragic cases and the others, or between those having higher or lower blood pressures. Appendectomy was routinely performed in all cases in which the organ had not been previously removed. In quite a few instances where other pathology was encountered multiple operations were performed, despite the fact that considerable bleeding had occurred into the peritoneal cavity. This pathology was not directly associated with the ectopic pregnancy, for example, myomas of the uterus, or cholecystitis with cholelithiasis. In all the instances of ruptured ectopic pregnancy or tubal abortions with hemorrhage into the peritoneal cavity, laparotomy was performed as soon after admission to the hospital as the patient could possibly be prepared.

We have analyzed and tabulated the leading signs and symptoms of our cases as follows: The outstanding symptom in all cases was abdominal pain. While this pain was occasionally generalized, in most instances it was localized to one side of the lower abdomen or suprapubically. It was present in 64 of the total number of cases. Amenorrhea was encountered in only 34 cases. Irregular menstruation followed by abdominal pain was noted in 25 instances. By irregular menstruation we mean that either the menstrual period began at the normal time, continued as a normal period but then instead of stopping was prolonged as spotting for an indefinite time, continuing from a few days to several weeks, or else the period, beginning at the normal time, was short and after a lapse of a few days continued again as spotting. Combining this irregularity with the cases which showed amenorrhea, in 59 instances there was a history of either a postponed period, prolonged period, or a skipped period. Spotting after amenorrhea, which is considered the typical irregularity of menstruation in ectopic pregnancy was found in only 37 of our cases. It seems very significant that in 7 instances there was no abnormality of menstruation whatsoever. Fainting occurred in 15 cases, nausea and vomiting in three cases, and distant pain, located in the clavicles, or in the shoulder blade was noted 6 times.

An analysis of the physical findings is as follows: In 29 cases pallor was manifest. Abdominal tenderness was present in 62 cases and abdominal spasticity in 42. Rebound tenderness was noted in 29 instances and a mass (palpable either

abdominally or on bimanual examination) was found in 42 instances. The cervix was tender on motion in 31 cases. Abdominal distention was present 4 times. The uterus was enlarged in 9 cases, 3 of which were cornual pregnancies. In 4 cases the hemoglobin ranged from 30 to 40, in 12 between 50 and 60, and in 13 it was between 60 and 70; in all the rest it was above 70 per cent. The estimations were all made immediately before operation. The following blood pressure readings were recorded at the time of operation or just before operation. Of the 60 tubal abortions or ruptured tubes, in only 25 was the systolic blood pressure found to be below 90 at the time of operation. Of these 25, 2 were so low as to be unobtainable by the ordinary sphygmomanometric method. In 4 the systolic was below 50. In 13, it was between 50 and 80. In 6 it was between 80 and 90. In the remainder the systolic blood pressure was above 90, just before operation.

The tabulation of the operative procedures is as follows: in 21 cases a simple salpingectomy with conservation of the ovary on that side was performed; in 5 salpingo-oophorectomy was done; in 22 instances a salpingectomy and appendectomy was performed; in 11 salpingo-oophorectomy and appendectomy was performed. In 10 cases the procedure was more complicated as follows, (A) salpingo-oophorectomy myomectomy and appendectomy (1 case); (B) salpingo-oophorectomy, sterilization of the opposite side, appendectomy (1 case); (C) salpingectomy, sterilization (1 case); (D) supracervical hysterectomy for unruptured cornual pregnancy with appendectomy (3 cases); (E) salpingo-oophorectomy and opposite side salpingectomy (1 case); (F) right salpingectomy, appendectomy and cholecystectomy (2 cases); (G) salpingo-oophorectomy, appendectomy and perineal plastic, (1 case). In this group of ten cases with the exception of the unruptured cornual pregnancies, there was considerable blood in the peritoneal cavity at the time the accessory operative procedures were performed. In both cholecystectomy cases separate right upper quadrant incisions were made.

At laparotomy, 31 tubal abortions, 29 ruptured tubes, including one ruptured cornual pregnancy, and 9 cases of unruptured ectopic pregnancy, of which 3 were cornual, were found. In 62 of the patients there was no other associated pathology besides the ectopic pregnancy. In 7, chronic salpingitis was found. In one there was a bilateral cystic oophoritis with tuberculosis of the tube. In one case there was a hydatid mole in the ectopic pregnancy, and also an associated cholelithiasis. In one case there was multiple fibromyomas, in another case there was cholelithiasis, and one patient had a pregnancy in a rudimentary horn of a uterus bicornis unicollis. This is of interest because of the possible etiologic relationship of associated pathologic lesions in the development of ectopic gestation.

The postoperative course in general was uncomplicated. There was one death. The case was one of a ruptured cornual pregnancy with considerable hemorrhage and shock. Intravenous glucose was given immediately upon admission to the hospital and continued throughout the operation. At the time of operation (it was performed without delay), the blood pressure was 90/50. The tube and the cornual portion of the uterus was excised and the cornual area closed by continuous suture. No other intraabdominal procedure was performed. During the operative procedure the patient developed circulatory failure but was resuscitated. However, about two hours after the operation the patient died in circulatory failure.

In twelve cases because of the poor circulatory condition of the patient, it was deemed necessary to give fluids intravenously before and during the operative procedure. This consisted of 5 per cent glucose solution to the amount of 1,000 c.c. Twenty patients received fluid parenterally, postoperatively. Three patients received whole blood postoperatively. In twenty-one cases the postoperative course did not require any parenteral fluid and was entirely satisfactory. One patient developed severe postoperative distention which yielded to treatment after a few days. An-

other was complicated by bilateral pyelitis and cystitis which cleared up upon treatment. There were no other significant postoperative complications. The average time in the hospital was two weeks.

Ectopic pregnancy is not a rarely encountered condition. According to E. A. Sehuman's statistics, its incidence relationship to that of normal pregnancy is 0.38 per cent. Keeping that in mind will be one of the greatest aids diagnostically.

For a full discussion of the etiology of ectopic pregnancy, reference should be made to the writings of Sehuman,<sup>1</sup> Wynne,<sup>2</sup> Farrar,<sup>3</sup> and Leith Murray.<sup>4</sup> In our series, in eight cases obstructive factors were found, seven cases of salpingitis and one case of tuberculosis of the tube. In none of the others was there any gross sign pointing toward any etiologic factor. Most ectopic pregnancies occur in multiparous women. This was not only true in our series but also found to be true by almost all contributors on the subject. It is generally agreed that once the diagnosis of ectopic gestation has been made, the patient should be prepared for laparotomy as soon as possible. There is still some difference of opinion regarding treatment after tubal rupture, the majority agreeing however, that immediate operation is preferable to any conservative treatment. The observation of Hunter Robb that severing the ovarian arteries of pregnant bitches did not kill the animals gave rise to the hibernation treatment of ectopic gestation.

The idea underlying the hibernation treatment is that the primary rupture, while possibly serious, is usually not fatal, since in the main, an arterial twig and not a large vessel is involved. According to this idea the bleeding continues until the blood pressure falls sufficiently for the formation of a clot and then the patient reacts, feeling well in a day or two. During the reactive stage the operation can be performed more safely. This particularly summarizes the teaching of the late Dr. John O. Polak. While this may be true of a large majority of cases, it certainly is not true of all. It is indubitably true that the majority of the patients *in extremis* do react and may be operated upon with comparative safety some time after the reaction. It is equally true, however, that no one can foretell whether the reaction will take place, or whether the patient will slip momentarily further and further beyond surgical aid and death end the scene without any more active attempt having been made to save the life of the woman than giving her morphine, hypodermic and proctoclysis and the Trendelenburg posture. While the resources of surgery are rarely successful when practiced on the dying, yet of all acute surgical conditions, ruptured ectopic pregnancy is one in which even when patients are operated upon almost in extremis, they recover with most surprising rapidity.

In the past the fear of operating was engendered by the idea that the operation added shock to an already existing shock, the combination of



which might prove fatal. In ruptured ectopic pregnancy, the picture is one of hemorrhage.

The hibernation treatment of ectopic pregnancy has frequently been advocated for the same reasons as those advanced for the expectant and palliative treatment of bleeding ulcers of the stomach. From a therapeutic approach standpoint the two are by no means comparable. In many instances of bleeding ulcer, it is impossible to find a bleeding vessel for ligation. Either the very extensive operation of subtotal gastrectomy or pylorotomy on an already exsanguinated patient must be performed or recourse must be had to gastroenterostomy, in the hope that drainage might indirectly favorably influence the hemorrhage. However, in the case of ectopic pregnancy the bleeding point is always accessible for easy ligation. From the standpoint of the therapeutic indication there is a very close parallelism between the hemorrhage of a ruptured tubal pregnancy and that due to slipping of a ligature on a vascular pedicle after laparotomy. In case frank hemorrhage were recognized post-operatively as the result of a slipped ligature what surgeon would hesitate to reoperate for the control of such hemorrhage?

Lilian K. P. Farrar<sup>3</sup> reported 3 deaths in 303 cases in all of which operation was not deferred. Scheffey et al.<sup>5</sup> report two postoperative deaths out of 82 patients operated upon immediately or within twenty-four hours. Leith Murray reports two deaths out of 146 patients similarly treated. In all these patients the authors explained their deaths as not being due to the operative interference but rather to some intercurrent accident such as postoperative pulmonary embolus on the eighth or tenth day or septic pneumonia.

An important factor in minimizing the trauma of the operative procedure in a woman already damaged by a severe intraabdominal hemorrhage, is the choice of subarachnoid block as the anesthetic. Maximal relaxation is afforded, which in turn insures easy, speedy operating with minimal tissue trauma. Shocking impulses generated in the operative field, blocked in the anesthetized spinal roots and cord, never reach the brain so that the central nervous system is spared. The fear that many of these patients already having a low blood pressure are not fit for spinal anesthesia because of its depressing effect on pressure, is entirely unwarranted. The Trendelenburg posture insures sufficient gravity drainage back to the heart to prevent its contractions on empty chambers, no matter how complete the peripheral and splanchnic vasodilatation be. Indeed, the lower the pressure before anesthesia, the less can the fall attributable to the anesthetic be. Although there were only 2 cases in this series in which no sphygmomanometric blood pressure readings could be obtained, we have operated on 6 other such cases due to tubal rupture, 3 cases of gastric ulcer hemorrhage, 1 case of traumatic rupture of the spleen, 1 case of laceration of the liver, and 1 case of laceration of the kidney. In these 12 cases also, sphygmomanometric readings were unobtainable because the pressure was so low. These ex-

periences in extreme cases, besides a familiarity with the uselessness of blood pressure readings as a criterion of a patient's condition during operation under spinal anesthesia gained in over 10,000 laparotomies, make us feel that ectopic pregnancy is not only no contraindication to the use of this anesthetic, but that it is suitable for use in this condition.

## REFERENCES

- (1) *Schuman, E. A.*: Extrauterine Pregnancy, 1923, D. Appleton and Co., p. 28.
- (2) *Wynne, H. M.*: Johns Hopkins Bull., January, 1919. (3) *Farrar, L. K.*: Am. J. Obst. 79: 1919. (4) *Leith, Murray H.*: Proc. Roy. Soc. Med. 25: 32, 1931.
- (5) *Scheffey, et al.*: AM. J. OBST. & GYN. 24: 103, 1932.

## OCCIPUT POSTERIOR

## A STATISTICAL STUDY FROM THE CHICAGO MATERNITY CENTER

JOSEPH G. CROTTY, M.D., CINCINNATI, OHIO

IN THE realm of obstetrics there is probably no topic which has been productive of more diverse and conflicting opinions than that supporting the methods advocated by various clinics in the management of occiput posterior positions. For this reason it is enlightening and helpful to review a large series of cases and thus to determine if possible wherein we have triumphed or failed. Many of these statistical studies are inaccurate for obvious reasons. The figures of hospitals are frequently at fault because they include a disproportionately large number of primiparas, in whom occiput posterior is generally recognized to be of more serious import than in multiparas; also because many patients are sent to hospitals only after attempts at delivery in the home have failed in the hands of the less skilled, or because dystocia is anticipated; and because operative interference is always more readily undertaken where it is more convenient. On the other hand, a series of cases taken from the private practice of trained obstetric specialists is apt to be equally misleading, since many cases fall into their hands only because they are pathologic and in need of skilled attendance. For the purposes of this study, we have selected the statistics of the Chicago Maternity Center, which is entirely an out-patient service, where all kinds of normal and operative obstetrics, with the exception of cesarean section, are undertaken in the homes. Hence, we believe this service is more likely to represent a cross-section of the general run of obstetric practice to be found throughout the country as a whole.

Most of the recent publications on this subject have shown a rather large proportion of operative deliveries. While these may be productive of good results in the hands of the skilled obstetrician in a well-equipped maternity, in the hands of the average practitioner, who still must do

most of his deliveries in the home, such interference will inevitably be unsatisfactory to say the least, at times even disastrous. A study of the figures about to be presented will reveal a tendency toward a strongly conservative attitude in our clinic, operative interference being resorted to only when strictly indicated, and then the interference in all cases is as radical as the circumstances require.

In presenting these statistics, there is, we believe, one figure which may well be challenged. Of the 7,803 deliveries in the twenty-nine-month period covered by this study, 6,223 are known to have been vertex presentations; and of these occiput posterior was diagnosed in 714 cases, an incidence of only a fraction under 11.5 per cent, which is one of the lowest on record. DeLee presents the statistics of the Chicago Lying-in Hospital as supporting an incidence of 12.1 per cent, and he quotes Karl Braun as giving the much larger figure of 30 per cent. Williams offers 20.8 per cent as his experience, and says that Plass was able to find only 11.1 per cent in 5,445 vertex presentations delivered at the Johns Hopkins Hospital. All of these figures, like our own, seem open to the criticism voiced by Danforth, who states: "In many services in which the observations are made and recorded by internes, the cases in which anterior rotation occurs are recorded as anterior positions, and the primary posterior escapes recognition." Danforth, by the way, says that occiput posterior has been encountered in 27.1 per cent of cases in his private practice, but this large incidence must fall under the objection we have already made to the statistics of the skilled obstetrician. In a small series of personally conducted home and hospital deliveries, I have recorded occiput posterior position in 28 per cent of vertex presentations, which seems unduly high. At any rate a mean of all these figures gives an incidence of 20 per cent, which seems to approximate the true state of affairs about as closely as possible.

Table I shows the incidence of the various presentations encountered on this service.

TABLE I. TOTAL DELIVERIES FROM JULY 1, 1932, TO DEC. 1, 1934, 7,803

Unattended (precipitated before arrival of doctor)	1,316	or 16.8%
Total attended deliveries	6,487	
Vertex presentations	6,223	96.0 %
Breech	222	3.4 %
Face and brow	23	0.35%
Transverse	19	0.29%
Total occiput posterior	714	11.5 % of all vertex cases
Occiput right posterior	489	
Occiput left posterior	225	
Primiparas	196	
Multiparas	518	

Of these 714 occiput posteriors, 614 or 86 per cent terminated in spontaneous delivery. On the other hand, if it is true, and in all likelihood it is, that 20 per cent of the 6,223 would be found to have been occiput

posteriors had more skill and care been employed in diagnosis and recording, then the operative incidence in this series is only 8 per cent, and 92 per cent of all our posterior cases have delivered spontaneously. Table II shows the frequency of the various modes of termination in the 714 deliveries.

TABLE II

Spontaneous rotation and delivery	573 or 80.2 %
Manual rotation, spontaneous delivery	3 or 0.42%
Spontaneous delivery, persistent occiput posterior	38 or 5.32%
Operative delivery	100 or 14.0 %

A review of the 100 operative deliveries reveals that all of them were strictly indicated interferences and also that by far the majority of them were difficult procedures. That the average length of the second stage in this group was 3.37 hours, with a mean first stage of 27.7 hours, will give some lead to the necessity of the operations done. In the nineteen cases in which dilatation of the cervix was completed by Dührssen's incisions, the first stage of labor averaged 48.5 hours, the longest being seventy-four hours and the shortest thirty-five hours. This operation is performed only under the most rigid indications, and then only when the proper conditions are present, and after the woman has had a fair test of labor with membranes ruptured, or when fetal or maternal distress demands rapid delivery before the cervix is completely dilated. All of these nineteen operations were performed upon primiparas. A statistical review of the 100 operations follows:

Total operative deliveries	100
Occiput left posterior	35
Occiput right posterior	65
Primiparas	85
Multiparas	15
Forceps Operations:	
High forceps (to be discussed later)	3
Midforceps	57
Low forceps	
After operative rotation	14
After spontaneous rotation	15
On after-coming head (version)	1
Key-in-lock maneuvers	26
Bill's Scanzoni modification	1
Failed forceps	1
Manual Rotation:	
Attempted	65
Failed	3
Succeeded	62
Version and Extraction	3
Dührssen's Incisions	19
Laparotrachelotomy	
1 primipara with cephalopelvic disproportion	
1 multipara with placenta previa totalis	
Craniotomy	5 (all on dead babies)

A close study of this summary of the operative work will demonstrate several very interesting points. In the first place, 70 per cent of all

these operations include high forceps, midforceps, version and extraction, craniotomy, or laparotrachelotomy, and only fifteen of the thirty low forceps were preceded by spontaneous rotation to an anterior position, which gives a good lead as to the urgent need of operative intervention. Another extremely interesting point is the success of manual rotation, which failed only three times in the sixty-five attempts, any manual rotation which effects a change to or beyond the transverse position being considered successful. Whatever may be said for or against this method by those who prefer forceps maneuvers, this much is certain, that rotation can be effected manually in the vast majority of instances, if it is persisted in by one familiar with the proper technique. We see also that forceps were used for rotation only twenty-seven times, twenty-six of these being key-in-lock maneuvers, most of which were utilized to complete a manual rotation which had already turned the head to or well beyond the transverse. The lone Bill-Scazzoni maneuver was performed upon a 335-pound multipara with a justo-major pelvis, who, because of uterine inertia and lack of cooperation, was unable to deliver spontaneously. Irregular fetal heart tones precipitated the decision to effect delivery, and the forceps were resorted to in preference to version, because the patient had a very bad upper respiratory infection, and it was deemed inadvisable to give her sufficient general anesthesia for the latter operation. Both mother and the baby made an uneventful recovery. In one of the other high forceps operations the baby died of cerebral hemorrhage; and the third was done on the after-coming head of a version and extraction, where cesarean section had been decided upon, but owing to failure of fetal heart tones while the patient was still at home, prompt delivery was resorted to, and both mother and baby are alive and well. It will also be noted that our methods differ from those of some clinics, in that all heads are rotated to the anterior position before the forceps are applied. In only one case was the head delivered in the posterior position, and that by a midforceps operation, both mother and child fortunately escaping injury.

Whether or not we are correct in our belief that all posteriors should be rotated before delivery is attempted, we must admit, is open to question. The recent work of Caldwell, Moloy, and D'Esopo upon the structure of the pelvis and the effect of its variations upon the course of labor seems to indicate that there may be certain cases in which the pelvis is best adapted to the passage of a posterior position. It will be noted that of the 614 spontaneous deliveries in our series, thirty-eight were expelled as persistent posteriors, many of them, even in primiparas, with surprising ease. This seems in some measure to bear out the contentions of those who advocate occasional extraction in the posterior position especially when the head has descended to the perineum, and it is probably best to try to learn which method promises the easiest delivery.

While we contemplate no change in our methods at the present time, we must acknowledge that the last word has not yet been spoken, and these new and interesting studies in the morphology of the female pelvis may some day cause us to change our minds about many things. Two of the versions were done upon multiparas with high occiput posteriors and both were productive of living babies; the third was done upon a premature infant with a prolapsed cord, and the baby lived only twenty-four hours. The two cesarean sections, as will be noted, were done for indications which made them absolutely necessary; the nineteen Dührsen's incisions have already been discussed, and indications for the five craniotomies will be brought out in the section on fetal mortality. Suffice it to say here that all of them were performed upon dead babies, as it is our policy never to permit the mother to suffer unneeded risk or damage for the sake of an infant that is known to have already succumbed.

We now turn to a discussion of our fetal and maternal mortality, but we shall not speak of morbidity, because in a service such as ours where temperatures are recorded as a rule only once daily, such observations are of little value. We can state empirically only that the incidence of febrile courses on our service seems to be unusually low, very few patients developing fevers which demand therapy of any kind. In the series of 714 occiput posteriors, we regret to report the death of one mother.

This patient was a twenty-five-year-old gravida ii who had had one previous spontaneous abortion. She had a mild case of pneumonia during her pregnancy, and from time to time complained of abdominal pain. She was delivered by manual rotation and midforceps, after which a severe postpartum hemorrhage necessitated manual removal of the placenta. Her puerperium was uneventful for the first eight days, and then she developed chills, fever, and a Bartholin abscess. This was incised and drained under a badly taken ether anesthesia, following which she developed pneumonia; she was sent to a hospital and died. Autopsy findings were those of a typical bronchopneumonia, such as is so frequently attributed to ether anesthesia. Incidentally this is the only maternal death that we have had on any of our operative deliveries since the beginning of the Chicago Maternity Center.

#### FETAL MORTALITY

There are seventeen fetal deaths recorded among the 714 deliveries, for a gross fetal mortality of 2.38 per cent; of these ten occurred in the operative series, making a gross operative mortality of 10 per cent. Deducting macerated babies, babies whose heart tones were inaudible when we arrived on the case, and others according to the indications outlined in the detailed account to follow, we have a corrected mortality of 1.54 per cent in the entire series, and the corrected operative mortality of 6 per cent, which is low enough considering the types of operatives involved. In this connection it must be emphasized that it is not our operative mortality that is to be considered, but the mortality of the entire

series, since a policy of intelligent expectancy seems to have been in large part responsible for the success obtained in the treatment of these cases. A detailed review of the fetal deaths follows:

- 2 Craniotomies on macerated babies; eliminated in corrected mortalities.
- 1 Craniotomy on fetus dead from long labor; included in both gross and operative mortalities.
- 1 Craniotomy on baby dead from complete abruptio placentae; included in gross and operative mortality.
- 1 Craniotomy on baby dead from failed forceps; included in both gross and operative mortality.
- 2 Died of cerebral hemorrhage after mid- and high forceps; included in both gross and operative mortalities.
- 1 Cause undetermined by autopsy, no evidence of cerebral injury; midforceps; death thought by mother to be due to accidental suffocation; may have been this or thymus; eliminated.
- 1 Second twin, single amnion and chorion with cords twisted and knotted together. Baby apparently died during labor; forceps; eliminated in operatives but included in gross.
- 1 Premature with prolapsed cord; died of cerebral hemorrhage after version and extraction; included in both.
- 1 Spontaneous delivery; persistent O.D.P.; died in thirty-six hours from cerebral hemorrhage.
- 1 Spontaneous; died in twenty-four hours. Autopsy; aortic occlusion, congenital.
- 1 Died in forty-eight hours. Melena neonatorum.
- 1 Cause undetermined, died eighteenth day; eliminated (Spont.)
- 1 Cause undetermined by autopsy; included in gross.
- 1 Stillborn; prolapsed cord; included in gross.

To recapitulate, a policy of intelligent expectancy was observed throughout the series of 714 occiput posteriors, interference being resorted to only where urgently indicated. The result, a fetal mortality of 1.54 per cent, speaks for itself; and while we do not claim that our methods are the "*sine qua non*" in the management of this very difficult problem, we are confident that our record should encourage their adoption by those who have been unable to find a system productive of results as good as or better than our own. This is no place to discuss operative technic, but it is only fair to state here that our problem in operative obstetrics in the home has been greatly simplified by the development of the parasaeral block technic as described by Tucker and Benaron, and for practically all of our operations this very efficient regional anesthesia gives ideal or at least satisfactory results. Manual rotation is rendered much more successful than under general anesthesia because of the greater relaxation secured, and the operation of Dührssen's incisions is made a comparatively easy procedure; even two of the three versions were performed quite successfully with this type of nerve block.

## SUMMARY

1. A series of 714 occiput posterior labors is presented with a corrected fetal mortality of 1.54 per cent and a maternal mortality of 0.14 per cent.

2. In this series operative intervention is undertaken in only 14 per cent, and in the 100 operative deliveries the gross fetal mortality was 10 per cent, and the corrected fetal mortality 6 per cent.

3. When operative intervention becomes necessary, manual rotation is considered the procedure of choice over the various forceps extractions, rotation being completed, when needed, by the key-in-lock maneuver with forceps. It is the policy to rotate all occiput posteriors to the anterior before attempting delivery.

4. It is estimated that occiput posterior positions occur in approximately 20 per cent of all vertex presentations.

5. Local anesthesia in the form of parasacral or pudendal blocks or combination of the two was employed successfully in practically all the operative deliveries.

3440 EDWARDS ROAD

## CESAREAN SECTION: FACTORS INFLUENCING MORTALITY

## AN ANALYSIS OF 243 CASES

A. TALBERT BOWERS, A.B., M.D., DAYTON, OHIO

**D**URING the past decade the literature has been replete with discussions of the use and abuse of cesarean section. It is generally agreed that cesarean section is a conservative procedure if the indications are adequate and if the operator is skilled. It is often upon the general practitioner, however, that the burden of decision first falls.

The object of this communication is to analyze in some detail the cesarean sections which have been performed at the Miami Valley Hospital, Dayton, Ohio, during the eight-year period from Jan. 1, 1926, to Jan. 1, 1934, and to determine as far as possible the factors which influence mortality.

## INCIDENCE OF OPERATION AND MORTALITY

As indicated in Table I, 9,527 women were delivered in the maternity division of the Miami Valley Hospital during the eight-year period. There were 243 cesarean sections, an incidence of one in each 39 hospital deliveries (2.55 per cent). The yearly operative incidence varies from 1 in 25 to 1 in 63 hospital deliveries. The operative mortality varied considerably from year to year. The mortality rate was highest (11.8 per cent) during 1930, even though the incidence of operation (1 to 39) was average for the entire series. The mortality rate was somewhat above the average during 1933, when the incidence of operation was lowest.



The classical cesarean section was done in 236 cases; the low cervical section in 3 cases; the Porro operation in 3 cases; and the vaginal section in 1 case. Ten of the 11 deaths followed the classical operation; one followed the Porro operation, which was complicated by previous rupture of the uterus with twin fetuses in the abdominal cavity.

TABLE I. YEARLY OPERATIVE INCIDENCE AND MORTALITY

YEAR	TOTAL DELIVERIES	CESAREAN SECTIONS	INCIDENCE OPERATION	DEATHS	PER CENT OF MORTALITY
1926	1,007	18	1 to 54	0	0.0
1927	1,110	20	1 to 38	0	0.0
1928	1,200	47	1 to 26	3	6.4
1929	1,313	52	1 to 25	2	3.9
1930	1,325	34	1 to 39	4	11.8
1931	1,305	27	1 to 48	1	3.7
1932	1,197	19	1 to 63	0	0.0
1933	1,070	17	1 to 63	1	5.9
Total	9,527	243	1 to 39	11	4.5

TABLE II. TYPES OF OPERATION

TYPE	NUMBER	INCIDENCE	PER CENT	DEATHS	INCIDENCE OF DEATH	PER CENT OF MORTALITY
Classical	236	1 to 1.03	97.1	10	1 to 24	4.2
Low cervical	3	1 to 81.0	1.2	0	0	0.0
Porro	3	1 to 81.0	1.2	1	1 to 3	33.3
Vaginal	1	1 to 243.0	0.4	0	0	0.0
Total	243		100.0	11	1 to 22	4.5

## INDICATIONS

TABLE III. INDICATIONS FOR CESAREAN SECTION

INDICATIONS	NUMBER	PERCENTAGE
Contracted pelvis	103	42.2
Dystocia	34	14.3
Previous cesarean	27	11.0
Placenta previa	16	6.6
Eclampsia	14	5.7
Preeclampsia	9	3.7
Malposition fetus	7	2.9
Rigid cervix	5	2.0
Bicornate uterus	4	1.6
Ruptured uterus	4	1.6
Prominent sacrum	3	1.2
Placenta marginalis	3	1.2
Previous third degree laceration	2	0.8
Heart disease	2	0.8
Acute nephritis	2	0.8
Fractured pelvis	2	0.8
Uterine fibroid	1	0.4
Thyrototoxicosis	1	0.4
Prolapse cord	1	0.4
Previous myomectomy	1	0.4
Old ulcerative colitis	1	0.4
Previous abdominal injury	1	0.4
Total	243	100.0

TABLE IV. MATERNAL MORTALITY

INDICATIONS	HOURS OF LABOR	MEMBRANE	VAGINAL EXAM.	CESAREAN OPERATION	ADDITIONAL OPERATION	ANESTHESIA	CAUSE OF DEATH
Contracted pelvis Previous cesarean	4	Intact	1	Secondary	None	Spinal	Anesthetic death
Contracted pelvis	3	Intact	2	Primary	None	Ethylene	Acute purpura hemorrhagica shock
Ruptured uterus	0	Intact	1	Secondary	Hysterectomy	Spinal	Subhepatic abscess. Pelvic abscess. Right pulmonary atelectasis
Contracted pelvis Breech presentation	11	Intact	1	Primary	None	Ethylene	Peritonitis. Toxemia of pregnancy
Bicornuate uterus Double genitalia	5	Ruptured	0	Secondary	Bilateral salpin- gitis	Ethylene	Postpartum hemorrhage. Purpura hem- orrhagica
Contracted pelvis Previous cesarean	3	Intact	0	Third	Steril.	Ethylene	Pneumonia
Dystocia	2	Intact	0	Primary	Bilateral salpin- gitis	Ethylene	Peritonitis. Incomplete closure wound. Pyeloneph.
Eclampsia	0	Intact	Insertion bag	Primary	None	Ethylene	Peritonitis. Ileus. Anuria
Contracted pelvis Face presentation	0	Intact	0	Primary	None	Nitrous oxide	Peritonitis
Dystocia	3	Intact	0	Primary	Bilateral salpin- gitis	Ethylene	Peritonitis
Dystocia	0	Intact	0	Primary	None	Ethylene	Cerebral embolism

In the analysis of the indications for operation, as recorded in Table III, an effort was made to group the cases according to the indications for operation. These data indicate that contracted pelvis still presents by far the most common indication for the cesarean operation. In most cases a trial of labor provided further evidence of contracted pelvis. Under the heading of dystocia was included disproportion of the size of the fetus and the pelvis. Inertia was also included under dystocia; no effort has been made to distinguish between primary and secondary inertia.

The dictum, "Once a cesarean, always a cesarean" appears to apply appropriately in all of the cases which were submitted to high classical cesarean section. It seems plausible that a patient who had previously been subjected to transverse cervical cesarean section would be less endangered during a subsequent trial of labor.

### ADDITIONAL OPERATIONS

Sterilization operations, usually salpingectomy, were performed in ninety instances (40 per cent). Even though the percentage of sterilization operations is high in this series, this was done because of the knowledge that the mortality rate is decidedly increased with each succeeding cesarean section on the same patient. Appendectomy was performed in five cases. Such incidental operations as myomectomy, oophorectomy, and repair of ventral herniae, were performed. It is apparent that additional operations should not be performed unless the patient's condition warrants the additional interference.

### GENERAL CONSIDERATIONS

The fetal membranes were ruptured before operation in 14 per cent of the cases. Vaginal examinations had been done prior to operation in 37 per cent of the cases. Delivery had been attempted by the application of forceps, insertion of bag, or version in 4 per cent of the cases prior to the performance of the cesarean section. Morbidity, which includes those patients with mouth temperature of 100°F. or more for over twelve hours, occurred in 40 per cent of the patients.

Information derived from the hospital records indicates that at least five of the patients who died following cesarean section had been subjected to vaginal examination prior to operation. The fetal membranes had been ruptured before operation in two cases. Seven of the patients had been in labor from two to eleven hours before operation. In one case a bag was inserted into the uterine canal before operation.

The mortality rate for persons who were subjected to a first cesarean section was 3.6 per cent; the mortality rate for those who were subjected to a second cesarean section was 7 per cent; the mortality rate was 20 per cent among those women who were cesareanized a third time. Vaginal examinations were done prior to operation in 37 per cent of the women in the entire series; vaginal examinations were done before operation in 46 per cent of the cases which ended fatally.

The average time for operation for the entire series was thirty-seven minutes, while the average operative time in the cases which ended fatally following operation was thirty-nine minutes. It seems probable that the operative time plays an insignificant rôle in the production of a fatal outcome.

Of the patients who died following operation, 73 per cent developed peritonitis, apparently produced by contamination from the vaginal outlet. The most frequent cause of such contamination was repeated preoperative vaginal examination, the use of douches, attempted delivery by forceps or bag, and lack of cooperation by the patient. It seems apparent that every obstetric case should be treated from the beginning of pregnancy as a potential operative case, thus avoiding contamin-

ation of the birth canal. Until this truth is realized the mortality rate in this country will remain excessive.

## FETAL MORTALITY

TABLE V. FETAL MORTALITY

DEATHS ACCORDING TO INDICATIONS		CAUSE OF FETAL DEATH	
	NUMBER		NUMBER PER CENT
Placenta previa	4	Premature	7 41
Abruptio placentae	3	Cause unknown	4 24
Eclampsia	3	Ruptured uterus	3 18
Ruptured uterus	3	Congenital syphilis	1 6
Prolapse cord	1	Pulmonary atelectasis	1 6
Dystocia	1	Hydrocephalus	1 6
Contracted pelvis	1		

Fetal mortality occurred in 7 per cent of cases, which include eleven stillbirths and six deaths following delivery. The corrected mortality of infants viable at birth was 2.45 per cent.

The fetal mortality in cases of ruptured uterus was 75 per cent, in placenta previa 25 per cent, and in eclampsia 21 per cent.

## ANESTHESIA

TABLE VI. ANESTHESIA MORTALITY

TYPE OF ANESTHESIA	NUMBER OF CASES	DEATHS	PER CENT OF MORTALITY
Ethylene plus oxygen	172	7	4.1
Nitrous oxide plus oxygen	38	1	2.6
Ether	21	1	4.8
Spinal	6	2	33.3
Avertin	1	0	0.0

Inhalation anesthesia was employed in nine of the eleven cases in which death was attributed to anesthesia. Spinal anesthesia was directly responsible for the death of one patient who died before the operation was begun. In the other case in which death followed spinal anesthesia the death was not in any way attributed to the anesthesia.

## CONCLUSIONS

1. Cesarean section is a conservative surgical procedure providing the indications are adequate and the operator is skilled.

2. The mortality rate shows a definite increase with each succeeding cesarean section.

3. Peritonitis, usually the result of preoperative contamination of the lower birth canal, is the most common cause of death.

4. The prenatal care of all pregnant women should include a consideration of the possibility that cesarean section might be required at the termination of pregnancy.

NOTE: The author wishes to express his thanks to Doctors E. R. Arn, R. C. Austin, B. W. Beatty, L. G. Bowers, R. A. Bunn, F. D. Crowl, R. K. Finley, G. C. Gillfillen, Curtis Ginn, H. H. Hatcher, H. H. Herman, J. K. Hoerner, E. M. Huston, H. R. Huston, M.D. Prugh, W. A. Ricketts, F. L. Shively, F. I. Shroyer, C. S. Smith, and R. H. Spittler for their kind permission to include in this study the records of patients admitted to the Miami Valley Hospital.

# FIBROMYOMA OF THE CERVIX UTERI\*

## REPORT OF CASE

VIRGIL S. COUNSELLER, M.D., AND DONALD C. COLLINS,† M.D.,  
ROCHESTER, MINN.

**T**RUE fibromyomas are occasionally seen arising from the cervix uteri that are of surgical significance.

Kolb found 5 (0.96 per cent) such tumors in a series of 552 cases of uterine fibromyomas. Boyd said that about 8 per cent of fibromyomas occur in the cervix. He also added that such cervical tumors were always single. According to Christopher, Bland-Sutton expressed the opinion that 5 per cent of all fibromyomas occur in the cervix. However, Vila and Schlossberg said that Schroeder gave the incidence as being 8 per cent, while Lee said that it was 15.5 per cent. Vila and Schlossberg in a series of 422 cases in which the uterus had been removed for multiple fibromyomas found only three (0.71 per cent) instances in which the cervix contained fibromyomas. Moench believed that 8 per cent of uterine fibromyomas occur also in the cervix. Turunen reported that 480 uterine fibromyomas were encountered at the gynecologic clinic at Helsingfors between 1919 and 1928, but that only two (0.42 per cent) of these occurred in the portiovaginalis. He said that Garkish found 1 per cent of uterine fibromyomas present in the cervix, while Albrecht, in 1928, found two cervical tumors among 700 specimens of uterine fibromyoma. Counsellor, Cox, Church and Paterson said that cervical fibromyomas may be found in 6 per cent of all diseased uteri which are removed surgically.

The literature on this subject is limited and consists primarily of isolated reports of cases. Turunen, in 1930, presented the only adequate review of the literature. He was able to collect 112 cases of fibromyomas of the uterine cervix and forty of these were first encountered when the tumor either blocked or rendered childbirth exceedingly difficult. He attributed the first report of a case to Langenbeck in 1859. Kolb, in 1910, found only twenty-four cases recorded in the literature and added five cases of his own, in one of which the tumor was responsible for an inversion of the uterus. Crousse, in 1922, described a huge tumor which measured 35 by 25 by 30 cm., and whose weight was 4,500 gm. Giles recounted an interesting case in which a large cervical fibromyoma had grown from the remaining cervical stump seven years after a subtotal abdominal hysterectomy had been performed for multiple uterine fibromyomas. The cervical tumor had rapidly filled the pelvis and had required prompt surgical removal. Moench also recorded a similar case in which the cervical tumor had appeared six weeks after operation for removal of another tumor. Solomons described the origin of a similar cervical tumor from the old scar in the anterior wall of the cervix, which marked an attempt to cure a sterility by dilating the ostia of the tubes from the vaginal route, which had been made several years previously.

Whitehouse<sup>21</sup> and Frommolt<sup>8, 9</sup> reported cervical tumors which were the cause of almost fatal vaginal hemorrhages. The case, which was reported by Hall, was remarkable because the tumor was so large that it filled the vagina and spread the

\*Submitted for publication, January 21, 1935.

†Now residing in Los Angeles, Calif.

vulva apart for a distance of 5 cm. Von Zur-Mühlen mentioned a similar case in which the cervical fibromyoma actually protruded from the vulva and the external portion measured 12 by 20 cm. The tumor in the case, which was reported by Kleff, was believed to have been a predisposing factor in the subsequent rupture of the uterus. Joseph, Zondek and Freund described an instance of a woman, aged thirty years, who had a cervical fibromyoma that blocked labor. Lehmacher reported two cases in which the tumors were intimately adherent to the bladder and hence were removed surgically with great difficulty. Courty, in 1932, recorded the instance of a large tumor, which arose from the posterior lip of the cervix and which was adequately treated by a total abdominal hysterectomy. The tumor in the case, which was recorded by Counsellor, Cox, Church and Paterson, was pedunculated, derived from the submucosa, measured 6 by 7 cm., weighed 230 gm., and was easily removed by local excision of the pedicle, followed by a perineorrhaphy. They said that Reel had previously described the largest cervical fibromyoma; it had pushed the fundus of the uterus cephalad as far as the level of the umbilicus and had weighed 7,000 gm. (15.4 pounds).

The factors responsible for the causation of cervical fibromyoma are not accurately known. These tumors commonly affect multiparas, but may not be discovered until they interfere with the course of labor. However, more commonly they occur at or soon after the menopause. Their first warning sign is frequently the appearance of a sudden large, often alarming, vaginal hemorrhage. The interstitial type of tumor frequently fills the pelvis, obstructing in varying degrees, the urethra, bladder, ureters, rectum, sigmoid flexure, and the birth canal. Neighboring structures in the pelvis may become densely adherent to the fibromyoma, making the surgical removal of the tumor both very difficult and exceedingly dangerous. Cervical fibromyomas may undergo degeneration, secondary infection or sarcomatous changes. Cabot<sup>2</sup> records a case in which a woman, who had a large cervical fibromyoma, also had an accompanying purulent streptococcic pelvic phlebitis.

Local removal of either the smaller interstitial or pedunculated subserous types of tumor through the vagina may be done sometimes with ease and safety. However, large interstitial tumors require an intra-abdominal approach, and total abdominal hysterectomy is usually the treatment of choice. Radium or roentgenotherapy may cause a temporary shrinkage in the size of the tumor, but should rarely be allowed to supplant adequate surgical removal. Cases which have been reported by Giles, Moench, as well as our case, amply support this contention. Fibromyomas of the uterine cervix appear to arise from either the anterior or the posterior lip of the cervix. Usually, these tumors are difficult to remove surgically and require the services of an experienced gynecologist to insure a favorable result. The reported operative mortality is around 8 per cent, while the postoperative morbidity is an appreciable factor.

The following is a brief report of a case of a large fibromyoma of the uterine cervix which was successfully removed surgically.

## REPORT OF CASE

A married Canadian woman, aged forty-nine years, was referred to the Mayo Clinic by her home physician because of a steadily enlarging mass in the lower uterine segment. She registered at the clinic on December 10, 1934. The family and past histories did not reveal anything important. There had been no previous operations. She had been well until two and a half years ago when she had had a marked vaginal hemorrhage. For the next six months she had had irregular menstrual periods which had been accompanied by "hot flashes" and small additional vaginal hemorrhages. Two years ago she had gone to her home physician for advice. He had performed a dilatation and curettage, which had failed to disclose any malignant changes. This had been followed by a course of roentgenotherapy. One



Fig. 1.—Anterior surface of uterus, tubes, and ovaries. It will be noted that the uterus sits on top of the cervical fibromyoma. The tumor can be seen emerging behind the greatly thinned anterior lip of the cervix and extending 11 cm. into the vagina.

month later she had had another severe hemorrhage. She had then been free from symptoms for the next six months, at the end of which additional vaginal bleeding had recurred. A second course of roentgenotherapy had been given at this time and she again had been well for five months. Since then, intermittent severe vaginal hemorrhages had occurred about every two months up to the time of her registration at the clinic. A third course of roentgenotherapy, together with the administration of calcium was given at home to prepare the patient for possible surgical treatment here.

Physical examination revealed a very obese woman who weighed 224 pounds (100 kg.) and who was 5 feet and 6 inches in height. There was extreme pallor of the skin. Soft blowing systolic murmurs were present at the mitral and aortic areas; they were not transmitted. There was a large firm mass in the lower part

of the abdomen. This was tender and extended to the level of the umbilicus. Vaginal examination disclosed a large mass which obscured the cervix. Rectal examination did not reveal anything abnormal. There were many large varicose veins and healed scars of old ulcers on the lower extremities.

The urine was alkaline in reaction and contained albumin 2 and leucocytes 1 (16 to each high-power field). The value for the hemoglobin was 9.5 gm. per 100 c.c. of blood. The erythrocytes numbered 3,980,000 and leucocytes 6,200 cells per cubic millimeter of blood. The Wassermann reaction of the blood was negative. Roentgenologic studies of the thorax revealed slight congestion of the base of the left lung.

On Dec. 11, 1934, the patient was operated upon. The abdomen was opened with a low midline incision. Multiple uterine fibromyomas, bilateral cystic oophoritis, bilateral chronic salpingitis, and a large fibromyoma of the cervix were discovered. The fibromyoma of the cervix measured 19 by 12 by 11 cm. (7.5 by 4.7 by 4.3 inches) and about half of it protruded through the external os. The patient also



Fig. 2.—Midsagittal section through uterus and huge fibromyoma of the uterine cervix, arising from the posterior lip.

had a chronic cholecystitis and cholelithiasis, but it was considered advisable to postpone cholecystectomy until a later date. The appendix was not disturbed. A total abdominal hysterectomy and a bilateral salpingo-oophorectomy were performed with considerable difficulty. Figs. 1 and 2 show the tissue which was removed.

The pathologist reported that the uterus weighed 2,095 gm. (4.6 pounds). The uterus contained multiple fibromyomas; the largest of these measured 19 by 12 by 11 cm. (7.5 by 4.7 by 4.3 inches), and the smallest measured 1 cm. (0.4 inch) in diameter. The largest tumor apparently had originated in the posterior lip of the cervix. It had produced a very marked dilatation of cervix, which was similar to that which occurs in a full-term pregnancy, and it had extended beyond the cervical lips for a distance of 11 cm. (4.3 inches). The tumor had encroached on the uterine cavity to the extent that the latter appeared only as a slit. There was atrophy of the tubes and ovaries.

The patient had an uneventful convalescence.



## REFERENCES

- (1) *Boyd, William*: Surgical Pathology, Philadelphia, 1925, W. B. Saunders Co., p. 488. (2) Case records of the Massachusetts General Hospital: *Graves, S. C., Hayden, E. P., McKittrick, L. S., and Mallory, T. B.*: New England J. M. 204: 728, 1931. (3) *Christopher, Frederick*: AM. J. OBST. & GYNEC. 11: 668, 1926. (4) *Counseller, V. S., Cox, F. W., Church, G. T., and Paterson, Susann J.*: Surg. Clin. N. Amer. 13: 966, 1933. (5) *Courty, Louis*: Bull. Soc. d'obst. et de gynéc. 21: 464, 1932. (6) *Crousse, René*: Gynec. et obst. 5: 84, 1922. (7) *Freund, R.*: Ztschr. f. Geburtsh. u. Gynäk. 100: 404, 1931. (8) *Frommolt, G.*: Zentralbl. f. Gynäk. 55: 2951, 1931. (9) *Frommolt, G.*: Ztschr. f. Geburtsh. u. Gynäk. 100: 402, 1931. (10) *Giles, A. E.*: Proc. Roy. Soc. Med. Sect. Obst. & Gynec. 16: 12, 1922, 1923. (11) *Hall, R. B.*: AM. J. OBST. & GYNEC. 7: 709, 1924. (12) *Joseph*: Ztschr. f. Geburtsh. u. Gynäk. 100: 404, 1931. (13) *Kleff, G.*: Med. Klin. 25: 1736, 1929. (14) *Kolb, Karl*: Ztschr. f. Geburtsh. u. Gynäk. 67: 399, 1910. (15) *Langenbeck, B.*: Quoted by Turunen. (16) *Lchmacher, Albert*: Zentralbl. f. Gynäk. 56: 2744, 1932. (17) *Mocnch, L. Mary*: Med. Clin. N. Am. 12: 1581, 1929. (18) *Solomons, Bethel*: Irish J. M. Sc. 5: 543, 1923. (19) *Turunen, A. O. I.*: Acta obst. et gynec. Scand. 10: 111, 1931. (20) *Vila, E. L., and Schlossberg, Teodoro*: Sémana med. 36: 344, 1929. (21) *Whitehouse, Beckwith*: J. Obst. & Gynec. Brit. Emp. 30: 211, 1923. (22) *Zondek, B.*: Ztschr. f. Geburtsh. u. Gynäk. 100: 404, 1931. (23) *Zur-Mühlcn, Friedrich von*: Zentralbl. f. Gynäk. 51: 2483, 1927.

## TUBAL GESTATION

### A STATISTICAL STUDY BASED ON 309 CASES

C. H. TYRONE, M.D., F.A.C.S., S. A. ROMANO, B.S., M.D., AND  
C. G. COLLINS, B.S., M.S., M.D., NEW ORLEANS, LA.

(From the Department of Gynecology, Tulane University, School of Medicine,  
and Charity Hospital)

IN REVIEWING 309 cases of ectopic pregnancy admitted to the Charity Hospital in New Orleans during the period from 1924 to 1934, the authors found that in this series there were 36 deaths in which the cause of death was directly attributable to this lesion. This mortality rate, 11.6 per cent, closely approximates the published mortality rate in acute appendicitis. Although acute appendicitis occurs much more frequently than ectopic gestation, certainly ectopic gestation carries just as high a mortality rate, and is invariably more difficult to diagnose. These incontrovertible facts prompted this study and analysis of cases. Before a study of this series was started, we were impressed, from the cases we had observed personally, with the fact that patients presenting the classical picture of ectopic gestation were greatly in the minority, and that the so-called atypical case was most frequently encountered.

That this idea was correct was borne out in the study of the present series. For this reason they were divided into an urgent group in which emergency operations were performed within the first twenty-four hours after the patient's admittance to the hospital, and a non-urgent group in which laparotomy was postponed until a later period.

One hundred thirty-three cases (43 per cent) fell under the caption of urgent cases, and 176 (57 per cent) under the grouping of nonurgent cases. In the urgent cases the preoperative diagnosis was ectopic gestation in 87 cases, or a correct preoperative diagnosis of 69.1 per cent, whereas in the remaining 46 cases the preoperative diagnosis was otherwise, usually acute appendicitis, or an error of 30.9 per cent. In the nonurgent group, 73 cases (41.2 per cent) were correctly diagnosed preoperatively, and 103 diagnosed incorrectly (58.8 per cent), the preoperative diagnosis varying from salpingitis to fibroids of the uterus.

We believe that the preoperative diagnosis of acute appendicitis in so many of the urgent cases can be attributed to the fact that in this series, in which the location of the pregnancy was definitely noted in 258 cases, 161 cases (62.4 per cent) were found to be in the right tube. The remaining 97 cases (37.6 per cent) were found in the left tube. This is not in accord with the conclusions drawn by Schumann,<sup>1</sup> from a study of cases reported by Castler, Farrar, Bovee, Frank, Foskett and Williams. However, we believe that the difference in this series is too great to be due to chance, and that ectopic gestation is most frequently found on the right side. No effort will be made to explain this difference, as any explanation would be purely hypothetical.

The authors are impressed by the large percentage of cases of salpingitis found, either microscopically or grossly, in this series. Eighty-five cases, or 27.8 per cent, showed microscopic evidence of tubal disease, while an additional 30 cases showed gross tubal disease in the uninvolved tube (9.7 per cent), giving a total of 37.5 per cent of tubal disease associated with ectopic pregnancy. This is in accord with the general observation of other authors that salpingitis is one of the most frequent etiologic factors in extrauterine pregnancy. Of late, reports have appeared in the literature of ectopic pregnancy following tubal insufflation, and we believe that such can be explained by a previous salpingitis, the insufflation merely reestablishing the lumen, so that conception can take place, but the peritubal adhesions and intramural changes are of such a nature that normal tubal peristalsis is interfered with and the lumen remains narrow enough to prevent the passage of a fertilized ovum.

The total number of cases reviewed is 309, with death in 36 cases, or a mortality of 11.6 per cent. Of the thirty-six patients that died, twenty-seven followed laparotomy, while nine patients died without surgical intervention. Autopsy in all nine of these cases showed massive intraperitoneal hemorrhage from ruptured ectopic pregnancy.

#### FATALITIES

1. Patient admitted, diagnosed as ruptured ectopic pregnancy, treated immediately for shock, but patient died before operation could be started. Autopsy, ruptured ectopic pregnancy.

2. Patient in hospital three days, apparently in good condition, waiting for donors so transfusion could precede operation. Died from sudden recurrent massive hemorrhage. No operation. Autopsy, ruptured ectopic pregnancy.

3. Patient admitted at 3 P.M., died at 8:30 P.M. same day. Admission diagnosis: Chronic salpingo-oophoritis, subacute appendicitis, secondary anemia. No operation. Autopsy, ruptured ectopic pregnancy.

4. Patient admitted with diagnosis of ruptured ectopic pregnancy, died two hours later during transfusion before operation could be started. Autopsy, ruptured ectopic pregnancy.

5. Patient admitted with diagnosis of chronic salpingo-oophoritis, possible ectopic pregnancy. Died four hours later. No operation. Autopsy, ruptured ectopic pregnancy.

6. Patient admitted with diagnosis of puerperal sepsis and bronchopneumonia. Died two days later. No operation. Autopsy showed ruptured right tubal pregnancy and bronchopneumonia.

7. Patient admitted with diagnosis of coronary thrombosis. Died three hours later. Autopsy, ruptured ectopic pregnancy.

8. Patient admitted with diagnosis of gastroenteritis. Died nineteen hours later. Autopsy, ruptured ectopic pregnancy, hemoperitoneum.

9. Patient admitted with diagnosis of possible ectopic pregnancy; possible pelvic abscess. Two days later developed cramps in the abdomen and died suddenly. Autopsy, ruptured ectopic pregnancy.

These cases illustrate that patients can and do die from ruptured ectopic pregnancy, as a result of massive intraperitoneal hemorrhage, and that there should be no "conservative" treatment in ectopic pregnancy.

#### CONCLUSIONS

1. The mortality rate in ectopic pregnancy closely approximates the mortality rate of acute appendicitis.

2. Ectopic gestation occurs more frequently in the right tube than in the left tube.

3. The diagnosis of ectopic pregnancy, ruptured and unruptured, is exceedingly difficult, due to the large number of atypical cases encountered.

4. Salpingitis is one of the most frequent etiologic factors in ectopic pregnancy.

5. There should be no conservative treatment followed in ectopic pregnancy. Immediate operation as soon as the diagnosis is established, and the shock from hemorrhage combated, is the only safe treatment.

#### REFERENCE

(1) *Schumann, E.*: Ectopic Pregnancy, Gynec. & Obst. Monographs, New York, 1921, D. Appleton & Co.

## MELANOMA OF THE URETHRA\*

ALEXANDER H. ROSENTHAL, M.A., M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology of the Long Island College Hospital)

**M**ELANOMA is an uncommon, highly malignant, generally pigmented neoplasm, arising usually from the choroid coat of the eye or pigmented nevi of the skin. Melanomas of the meninges, rectum, adrenal, and vulva are on record. Origin from the region of the external orifice of the female urethra is a most unusual site and warrants report of this case.

A search of the literature revealed four similar cases,<sup>1, 2, 3, 4</sup> but cursory mention of melanoma of the urethra was noted in two large reported series of melanomas.<sup>5, 6</sup>

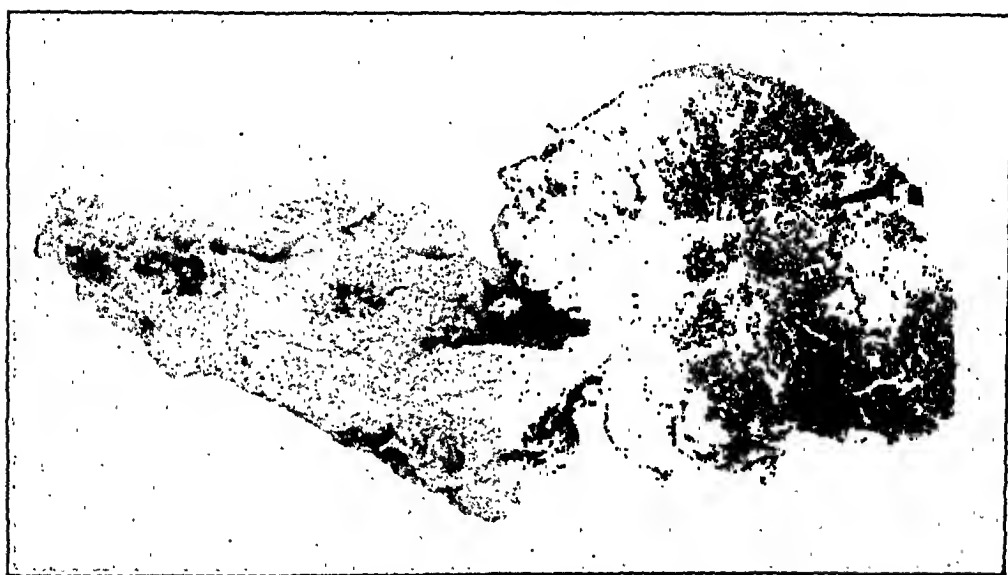


Fig. 1.—Sagittal section of the gross specimen. The pale pedicle, derived from the urethra, shows irregular darker areas. The main mass is the tumor proper. It is compact, dark and is invaded by branches from the pale central stromal core.

In one of these<sup>4</sup> it is doubtful whether the melanoma was primary in the urethra. Our observations together with those noted in the literature show this peculiar tumor to have the following characteristics:

1. It occurs in the aged. The average age for the five cases is seventy years, the youngest sixty-four years and the oldest seventy-five years.

2. Vaginal discharge and urinary symptoms occur but are not constant. In three cases a bloody discharge was observed, in two, dysuria was present, and two patients noted the presence of the tumor.

3. In every instance the tumor arose from a portion of or the entire tissue surrounding the external orifice of the urethra. Yet in no case was there complete urinary obstruction. In only one instance was the urinary stream diverted.

Miss K. F., a seventy-five-year-old spinster, was admitted on Jan. 7, 1935, to the Gynecological Service of The Long Island College Hospital. The patient first noted

\*Read before the Brooklyn Gynecological Society, March 1, 1935.

a foul-smelling, coffee-colored mucoid vaginal discharge about six weeks prior to admission. Within a few days this became grossly bloody. Two weeks later a brother noted that she did not appear well. Her weight decreased from 97 to 90 pounds. She also had a slight cough.

On examination she appeared seuiile, emaciated, but not acutely ill. Her vision was good and no abnormalities were noted in the fundi, except for the vascular changes characteristic of senility. The chest was emphysematous, the heart slightly enlarged, and the spine moderately scoliotic. The liver was not palpable. A pink, pedunculated verrucous growth, measuring  $1\frac{1}{2}$  cm. in diameter was noted on the skin in the region of the left lower abdomen, and a firm, almond-sized lymph node was revealed on deep palpation in the left inguinal region. Several other smaller nonpigmented verrucous growths of the skin and hemangiomas were also observed.

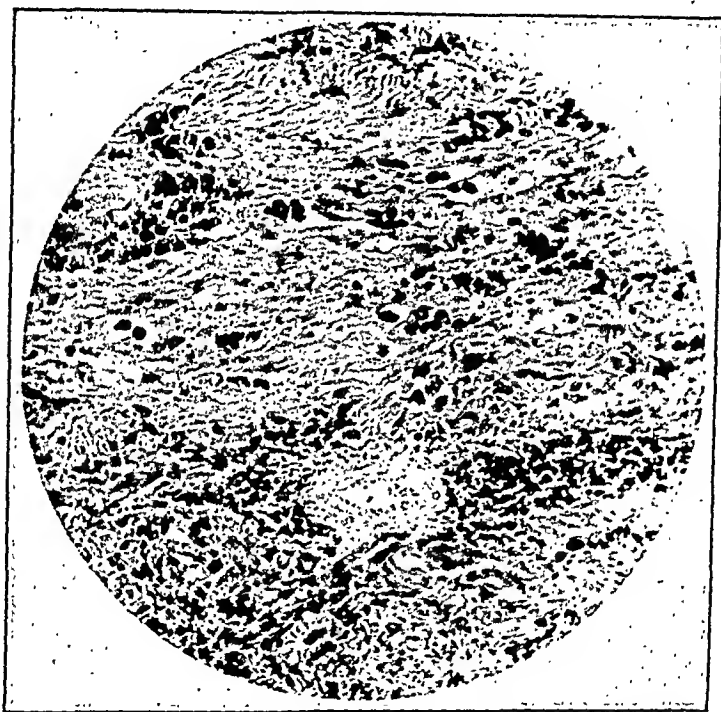


Fig. 2.—Spindle-shaped cells resembling sarcoma are seen. Adventitial cells surrounding the blood vessel are loaded with melanin pigment. (X200.)

The laboratory findings were essentially negative. Roentgen examination of the chest and bones showed no evidence of metastases.

A satisfactory pelvic examination could not be made until the patient was narcotized with morphine and scopolamine in preparation for the operation. At this time an irregular pedunculated cauliflower growth,  $3\frac{1}{2}$  cm. in diameter, was seen arising from the region of the urethral orifice. Externally the friable tumor was purple-black in color. After inserting a glass catheter into the bladder, the mass was seen to arise from the region of the external orifice of the urethra and not from the mucosa of the vestibule. This was further proved by traction on the growth which revealed its attachment to the terminal portion of the urethra. Rectal examination disclosed the cervix to be posterior and mobile. The uterus was atrophic and the adnexa and parametria were not palpable.

On Jan. 10, 1935, under morphine scopolamine narcosis and local anesthesia, the mass was excised with an electrocautery. The postoperative course was essentially

uneventful. She was out of bed on the ninth day and home on the seventeenth day. Examination at the time of discharge showed a granulating wound. A follow-up report on Feb. 25, 1935, revealed the patient to be feeling well. There were no urinary symptoms nor recurrence of her vaginal discharge and bleeding.

*Pathologic Report.*—The specimen consisted of an irregular tissue fragment which measured 32 by 26 by 15 mm. and was necrotic in portions. The main mass was lobulated and bluish-black. The pedicle was greyish-white and showed small irregular darker areas. On section, a pale central stromal core was observed to arise from the pedicle. This was subdivided into small branches which penetrated the main mass in all directions.

*Microscopic Examination.*—The sections revealed the tumor and an adjacent segment of urethra. The latter was normal except for focal hyperkeratosis. The tumor mass was comprised of groups of malignant spindle and polygonal cells separated

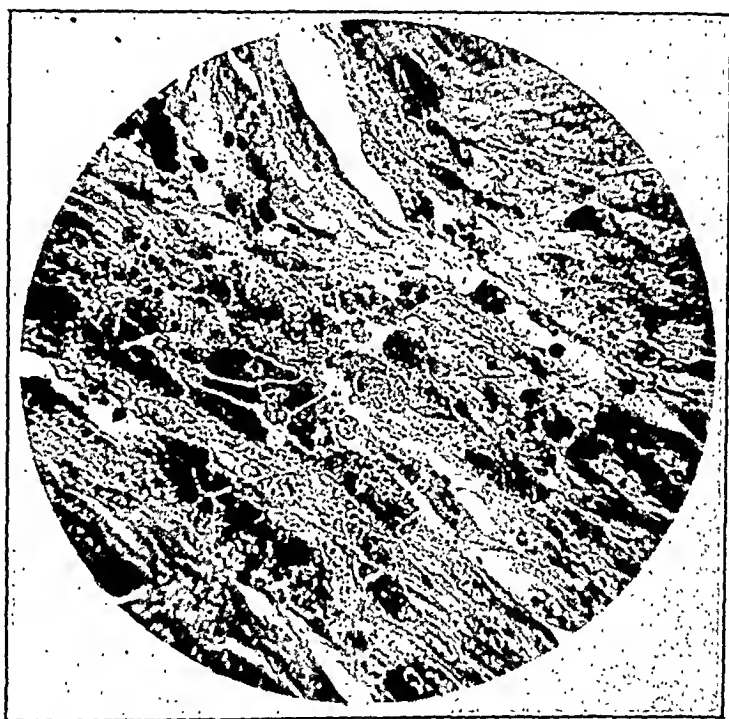


Fig. 3.—The large spindle and polygonal malignant cells show many granules of pigment in their cytoplasm. (X800.)

into irregular alveoli by narrow strands of hyalinized connective tissue. The malignant cells presented a poorly defined cell membrane and an elongated nucleus with a fine chromatin network. In the connective tissue septa, round and oval cells carried deposits of melanin pigment. The pigment was irregularly arranged in coarse round granules which in some areas were massed together. In many of the cells of the tumor proper, pigment deposits were also seen. A diagnosis of melanosarcoma was made, and further confirmed by excluding hemosiderin pigment and by the bleaching test.

Melanomas of the vulva have been reported much more frequently. In 1920, Kehrer<sup>7</sup> collected 83 cases from the literature. Their average age was fifty-four years. In these patients the clinical course was characterized by ulceration, lymphatic involvement and occasionally, widespread metastases. Since the external orifice of the urethra has somewhat the same anatomic relations as the clitoris and labia

minora, from which many of the tumors collected by Kehrer arose, we might expect a similar picture in our patient. Her senility, however, may be a factor in retarding the activity of the growth.

I am indebted to Dr. B. A. Harris for his kind permission to report this case and to Dr. S. A. Wolfe for his aid in the study of the pathology of this interesting tumor.

#### REFERENCES

- (1) *Koerner, J.*: Zentralbl. f. Gynäk. 51: 834, 1927. (2) *Sanger*: Geburtsh. Gyn. Ges., München, January, 1924. Ref.: Monatschr. f. Geburtsh. u. Gynäk. 66: 177, 1924. (3) *Read, C. A. L.*: Am. J. Obst. & Dis. Women 34: 864, 1896. (4) *Kustner, O.*: Kurzes Lehrbuch der Gynäkologie, Jena, p. 76, 1912. (5) *Broders, A. C., and MacCarty, W. C.*: Surg. Gynec. Obst. 23: 28, 1916. (6) *Hinselmann, H.*: Ztschr. f. Geburtsh. u. Gynäk. 62: 34, 1908. (7) *Kehrer*: Stoeckel's Handbuch der Gynäkologie 5: Part I, 496, 1920.

350 HENRY STREET

### INTRAVENOUS ANESTHESIA WITH EVIPAL SOLUBLE\*

ALBERT HOLMAN, M.D., AND ALBERT MATHIEU, M.D., PORTLAND, ORE.

WE WISH to report the use of "Evipal Soluble" as an intravenous anesthetic in one hundred gynecologic patients. Forty-six of these were private patients and fifty-four were from the gynecologic service of one of us (M) at the Multnomah County Hospital.

Evipal soluble is the sodium salt of N-methyl-cyclohexenyl-methyl-malonyl-urea. It is supplied as a powder in ampules containing 1 gm. accompanied by an ampule of 10 c.c. of distilled water in which the powder is to be dissolved shortly before use. When administered intravenously, evipal soluble has an extremely rapid effect, and since it is not a volatile substance, the anesthetic must be defined as uncontrollable. However, the detoxication proceeds so rapidly that it approaches closely controllable anesthesia in the ebbing of its effect. The detoxication is due to its chemical decomposition in the body, especially in the liver. The lethal dose has been determined to be from three to four times the full anesthetic dose. Surgical anesthesia is produced very rapidly.

#### ADMINISTRATION AND DOSAGE

Evipal soluble is administered intravenously, preferably in the median basilic vein. No preliminary medication is necessary. The recommended dose is 1 c.c. of a 10 per cent solution (obtained by dissolving 1 gm. of the drug in 10 c.c. of distilled water) for each 16.6 pounds, with a maximum dose of 10 c.c. at one time. The length of the contemplated operation affects to some extent the amount of the drug to be administered.

Evipal soluble has been used extensively in Europe, and many writers have reported large series of cases without fatalities. A total of these reported cases amounts to over 50,000, and in only one of these could the death be attributed to the drug. The British Medical Research Council has made an extremely favorable report on the safety of evipal soluble.

\*Submitted for publication, February 6, 1935.

## LIST OF OPERATIONS

Vaginal examination under anesthesia	7	Cauterization of Bartholinian gland	7
Dilatation of cervix	5	Cystoscopy and pyelogram	1
Curettage	40	Rectal abscess	1
Therapeutic abortion	6	Dilatation of rectum	2
Cauterization of cervix, cysts, and polyps	10	Hemorrhoidectomy	1
Excision of rectal fistula	3	Needling culdesac and colpotomy	5
Excision of rectal ulcer	5	Salpingectomy and suspension of uterus and appendectomy	1
Incision and suture of perineum	1	Removal of large tumor from labia with cautery	1
Perineal repair	1	Cautery vaginal wall cyst	1
Cauterization of venereal warts	3	Removal of vaginal septum	1
Simple amputation of breast	1	Urethral fibroma	1
Breast abscess	1	Cautery Skene's glands	1
Biopsy	4		
Separation of adhesions about clitoris	1		

Eleven patients had more than one operation.

It has been advised that from one and one-half to two minutes be taken for the injection, but it was our experience that anesthesia occurred more quickly and seemed to last longer if the drug was given at a more rapid rate. As our experience with the drug progressed, the time occupied in the injection became shorter, and we feel at present that thirty seconds is the best length of time to use in injecting the solution. It is important that the jaw be supported during the injection and while the patient is asleep. We instructed many of our patients to count slowly, and we found that they stopped counting and were asleep in from twelve to twenty-five seconds. The rapidity of the anesthetic effect seemed to depend upon the rapidity of the injection. The anesthetic effect lasted from ten to fifteen minutes, depending upon the amount of the drug administered and on the speed with which it was given. At times we injected the optimum amount, and then later, if the operation took longer than had been anticipated, we injected another 2 or 3 c.c. at the first sign of movement.

Blood pressure readings were taken preoperatively and five, ten, and fifteen minutes after the injection; and it was our experience that the majority of patients showed a moderate drop in both the systolic and the diastolic pressure in five minutes with a gradual return to the preoperative level. The pulse was recorded at the same interval, and most of the patients showed a moderate increase of rate at the end of five minutes. This gradually dropped to the preoperative rate. The respirations became slower and deeper.

The pupils became widely dilated by the time the injection was completed and responded to light in about seven to ten minutes. Seven of the one hundred patients were somewhat nauseated upon awakening and of these, four vomited. Vomiting was avoided if the injection was given to the patient when the stomach was empty.

As a rule, the patients aroused, that is, began to move, in from ten to twenty minutes and were awake in from fifteen to thirty minutes; however, these patients were variable in conduct. Some awakened in a shorter time, and an occasional patient slept longer than thirty minutes. Most of the patients operated upon in the office were able to leave in from one and one-half to two hours, but were somewhat sleepy during the remainder of the day.

One operation, consisting of salpingectomy, suspension of the uterus and appendectomy, was commenced with the patient under evipal soluble anesthesia. At the end of fourteen minutes, the administration of nitrous oxide was begun and continued throughout the remainder of the operation. The blending of the two anesthetics was smooth, and very little of the gas was required to complete the operation.



When they awakened, several of our patients did not believe that they had been asleep or that the operation had been performed. We mention this to demonstrate the amnesic effect of the drug. Most patients seemed to awaken in the same state of mind as that in which they went to sleep. If they were nervous and excitable before the injection, they awakened nervous and excitable. For this reason, we found that it was advisable to reassure the patient and to establish composure before the evipal soluble was injected. A number of the patients who were instructed to count during the injection and who went to sleep counting, continued to count when they awakened, starting where they had left off upon losing consciousness. Patients seemed to awaken more tranquilly if they were left alone and not disturbed. The effect of evipal soluble seems to be such that a period of time lasting from ten to thirty minutes was removed from the patients' consciousness, during which time there was complete surgical anesthesia and amnesia without any exciting or untoward effect.

#### CONTRAINDICATIONS

Contraindications to evipal soluble narcosis have not been established to date. It is obvious that aged, cachectic, debilitated, and seriously ill patients, and those suffering with severe circulatory or respiratory diseases should be treated with the necessary individual caution. Since evipal soluble is detoxified in the liver, special caution should be observed in its use when there is liver damage. As one would suspect, the narcosis would be prolonged.

#### CONCLUSIONS

In evipal soluble anesthesia we have an intravenous anesthetic of real value, which has been completely satisfactory in our hands. It gives surgical anesthesia and absolute relaxation for a period of time varying from ten to fifteen minutes. This anesthesia and relaxation can be continued for several minutes longer by the additional injection of 2 or 3 c.c. of the solution. The anesthesia is so profound that the abdomen may be opened or the rectal sphincter dilated. Any simple laparotomy not requiring more than twenty minutes can be done with this anesthetic, if, at the end of ten or twelve minutes, an additional 2 or 3 c.c. of evipal soluble are injected. We suggest this anesthetic as an especially good one for short operations on tuberculous patients. We experienced no disagreeable or dangerous effects in our series of one hundred cases, and we heartily recommend it as the anesthetic of choice for most surgical operations that can be done within fifteen minutes.

# ROUTINE TREATMENT OF GONORRHEA IN FEMALES

## NONANTISEPTIC METHOD

BERNARD NOTES, M.D., WASHINGTON, D. C.

*(From The Department of Obstetrics & Gynecology, School of Medicine, The George Washington University, and The Social Hygiene Clinic, Health Department of the District of Columbia)*

THE negativistic policy of some public health officials who hold that gonorrhea is often a self-limited disease of short duration, and the unphysiologic therapeutic attitude of many practitioners, warrants this analysis of the good results obtained during a period of eighteen months by a combination of methods based on an understanding of the anatomy, physiology and pathology of the female generative tract, with its variations during the whole life of the female.

The following is generally held by gynecologists:<sup>1</sup> (a) the fountain-head focus is in the cervix; (b) the next most important focus is in the urethra (Skene's ducts and paraurethral ducts) which is lined by resistant stratified squamous or transitional epithelium; (c) the vagina, during the reproductive period, suffers only transiently; and (d) the upper genital tract tends to resolve itself of infection if relieved of the reinfection and constant drainage from the lower genital tract.

This analysis covers the work of the Gynecological Section, Social Hygiene Clinic of the Health Department of the District of Columbia during the past four years, but particularly the last eighteen months. During this period 2,129 new positive cases of gonorrhea of the female genitalia were admitted for treatment. Obviously, the usual difficulties attendant upon a City Social Hygiene Clinic along lines of continuity of treatment and follow-up were encountered due to the type of patient.

Positive diagnosis was based on smears with gram-negative intracellular diplococci having the morphology of the gonococcus, plus objective clinical signs. While not taken as diagnostic, extracellular gram-negative diplococci were considered as suspicious, and no patient was discharged as recovered who had these suspicious smears. In order to discharge a patient as cured, four consecutive smears negative for both intra- and extracellular gram-negative diplococci obtained at intervals of two weeks with absence of objective clinical signs was required. Thus each patient was observed two months for recurrences.

The basis of treatment in the beginning was drainage and antisepsis. In 1931 antiseptics used in treatment included iodine and lysol, as douches and by topical applications, and of 384 cases admitted, four were discharged, 1 per cent. In 1932 antiseptics used included iodine,

lysol, mercurchrome and silver nitrate (10 per cent.) and of 522 patients admitted, 18 were discharged, 3.4 per cent. In 1933 of 546 cases admitted, 48 were discharged, 8.7 per cent. In August, 1933, the direction of this particular phase of venereal disease work was put in the hands of a gynecologist. Treatment on the bases of creation of local reaction and drainage with the omission of antiseptics was begun as follows: (a) all cervixes with cervical glands functioning<sup>2</sup> were cauterized one or more times with the electrocautery at intervals of two or more months in order to cause local reaction and to give better drainage of the active focus; (b) urethral meatus and cervix were treated weekly with applicators saturated with 25 per cent silver nitrate (considered a local irritant, not an antiseptic, in this strength) in order to cause local reaction and to favor better drainage; (c) 5 per cent sodium-bicarbonate douches were

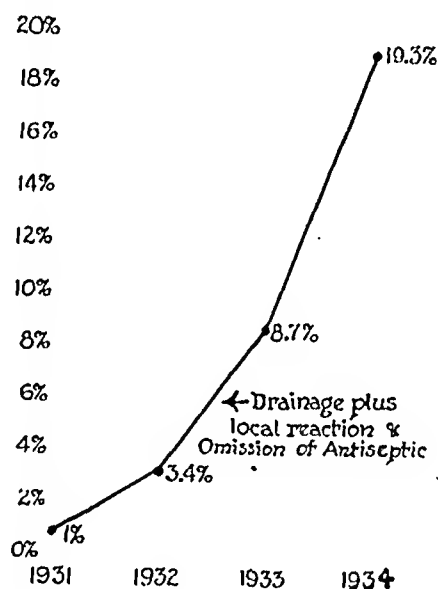


Fig. 1.—Showing effect of treatment in percentages.

taken by the patient at home twice daily, by fountain syringe until the cervix healed and by pressure syringe (bulb type) after the cervix healed; and (d) nightly instillations of 1 dram of 1 per cent lactic acid jelly were made by nozzle to the vaginal vault in order to promote the normal bacterial flora and to get rid of secondary invaders which cause desquamative vaginitis. During the first six months of this period, but twelve patients were discharged; however, clinical improvement and increase in negative smears were marked. Beginning with February, 1934, sustained results began to be obtained, and of 677 cases admitted during the following twelve-month period, 131 were discharged, 19.3 per cent. In other words, in 1931, 1932, and 1933 combined, but 110 were discharged as against 131 for 1934 alone.

Ages of patients ranged from a few weeks to sixty years, the average being nineteen years of age. Approximately one-half had syphilis which

was under active treatment. The largest number of cauterizations upon a single patient was 5, the smallest 1, and the average 2. Total number of cauterizations during the eighteen-month period was 786. Some cases which had resisted treatment by antiseptics for as long as four years were cured within one year by creation of local reaction and drainage. No patient who cooperated failed of cure.

Complications such as pelvic peritonitis and hemorrhage were at times severe but at no time dangerous; and these did not develop often. Patients were prepared for these reactions by a thorough explanation of what was being done, why, and what was to be expected. Occasional incomplete stenosis of the cervix developed as was expected but no cases of hematometra. One abortion occurred in an early pregnancy which was not diagnosed at the time of electrocauterization of the cervix, but good recovery resulted.

#### CONCLUSIONS

1. Antiseptics should be abandoned in the treatment of gonorrhea in females.

2. Cure lies in a physiologic-pathologic approach and consists mainly of creation of local reaction and drainage.

#### REFERENCES

(1) *Frank, Robert T.*: Gynecological and Obstetrical Pathology, ed. 2, 1931, D. Appleton Company. (2) *Notes, Bernard*: J. A. M. A. 100: 1103, 1933.

1801 EYE STREET, NORTHWEST

---

**Burch, Phelps, and Wolfe: Endometrial Hyperplasia, Arch. Path. 17: 799, 1934.**

The authors particularly call attention to a method of diagnosis previously described by the senior author. This consists in removal of endometrial tissue for histologic study by a "punch" and suction and, if their belief, is superior to curettage. Serial sections from several areas in the endometrium, taken as near the onset of menstrual bleeding as possible, reveal very interesting information.

A fungus appearance of the endometrium must be differentiated from carcinoma. These studies, as verified by others, seem to show that there is no tendency for the lesion to merge into carcinoma. Hyperplasia may occur at any time of life; it is more frequent at or near the menopause. Vaginal bleeding is the chief symptom. The lesion must be further differentiated from abortion, fibroid, unruptured ectopic pregnancy and luteal polymenorrhea. Careful history and physical examination will often lead to correct diagnosis. The prognosis of the disease as regards life is good; although some fatal cases have been reported. Pregnancy may occur after a spontaneous recovery. The disease is amenable to treatment with hormones, radiotherapy, curettage, or hysterectomy. Anterior pituitary hormones give encouraging results. Parathyroid extract (Collip) has been useful in some cases. Radium and roentgen rays are very useful near the menopause. In young patients curettage should be repeated before a more radical form of treatment is instituted.

W. B. SERBIN.

## OBSERVATIONS ON THE NORMAL SEX RATIO OF ALBINO RATS AND THEIR ARTIFICIAL VARIATION

MIHRAN A. VARZHABEDIAN, M.D., CHICAGO, ILL.

THE following theoretical outline has been taken as a working basis for the experiments performed:

1. That chromosomes of the sperms are the determinants of sex.
2. That sperms are of two kinds, one containing the X element and one without the X element.
3. The sperm with the X element uniting with the ovum having its constant X element, produces a female while ova uniting with sperms without the X element produce males.
4. The action of the X element is quantitative.

Taking the above points which were brought out by Prof. E. B. Wilson of Columbia as a foundation and assuming that the quantitative increase in the chromosomes is closely related to the physiologic activity of the organism in general and the sex organs in particular, I have utilized depressants for the production of chromosomes without the X element and stimulants to produce chromosomes with the X element for the production of males and females, respectively.

The experiments have been carried out on the following plan: The male rats have been kept in separate cages and gradually saturated with the medication desired for varying periods from two weeks to ten weeks, then mated with the females and after impregnation the females segregated in individual cages and the litters checked and recorded. It has been observed that there is a definite increase of the desired sex in the litter if the male has been kept saturated with the medication longer.

The normal sex ratio of the albino rat, as quoted by Richard Goldschmidt in his book on *The Mechanism and Physiology of Sex Determination*, is 100 females to 105 males, there being a slight increase of females during the summer months and of males in the winter.

The experiments were started during December, 1927, and have been followed at varying periods depending upon the facilities at hand. The medication used included the bromides for the male experiments and thyroid, pituitary and testicular extract combinations for the female experiments. All rats under observation were fed the same mixtures of different food elements.

The following results have been observed in the experiments performed in the first series. A new series is at present started in the Pathological Laboratory of the Martha Washington Hospital.

TABLE I\*

MEDICATION	PARENTS		DATE OF BIRTH	LITTER	RATIO		LENGTH OF MEDICATION
	M.	F.			M.	F.	
M	A	E	March 16, 1928	6	5 - 1		Days
M	A	E	May 5, 1928	8	6 - 2		21
F	A	E	June 20, 1928	7	1 - 6		21
F	C	F	March 22, 1928	9	2 - 7		28
M	C	F	May 8, 1928	9	7 - 2		21
M	C	F	July 4, 1928	9	8 - 1		15
F	C	F	Aug. 2, 1928	13	6 - 7		
F	G	H	July 25, 1928	6	2 - 4		
M	G	H	Oct. 4, 1928	6	5 - 1		
F	X	Y	May 18, 1929	7	1 - 6		
M	X	Y	July 31, 1929	8	6 - 2		
M	V	W	May 22, 1929	6	4 - 2		
F	V	W	Aug. 1, 1929	9	2 - 7		
M†	O	P	July 13, 1929	8	8 - 0		10 weeks

\*The letters in the first column indicate the medication used, M for male, showing that the male rat has been fed so as to produce more males in the litter and F for females.

The second column shows the parents used in the experiments.

The third column gives the date of birth of the litter.

The fourth gives the total in the litter.

The fifth gives the ratio of the sexes in the litter.

The sixth shows the length of medication of the male rat.

†The feeding of this male rat was started when he was yet three weeks old and continued until maturity when he was mated with his litter mate. The result gave 8 males with no females in the litter. It will be noted that the shorter the period of feeding of the male the closer to the normal ratio of the sexes in the litter. The rest of the experiments have been for males or for females directly without using the same pairs for shifting the ratio. The male experiments with the use of the bromides have given uniformly satisfactory results. The influence of season and diet has made no change in the proportion. In the direct experiments with the stimulants for the increase of females in the litter the results have not been as high as in the male experiments, the total ratios standing 62F:28M for the female experiments and 87M:29F for the male side, total number of litters obtained to date being 37.

The figures in Table I are given as observed without any comment.

2700 DEVON AVENUE

Mazza and de la Colina: Hydatidiform Mole and Chorionepithelioma, Bol. Soc. de obst. y ginec. 13: 677, 1934.

The authors report three cases, one of hydatidiform mole, one of chorionepithelioma, and one of doubtful clinical entity, diagnosed by the use of the biologic test of Aschheim and Zondek used in minute doses. These cases were followed up with the same technic for evidences of recurrence.

MARIO A. CASTALLO.

# A SIMPLE ROENTGENOGRAPHIC METHOD FOR ACCURATELY DETERMINING THE TRUE CONJUGATE DIAMETER OF THE PELVIS

SAMUEL F. WEITZNER, M.D., NEW YORK, N. Y.

*(From the Morrisania City and Lebanon Hospitals)*

THE purpose of this paper is to describe a new method of measuring accurately the true conjugate diameter of the pelvis by means of a simple roentgenographic procedure. To the best of my knowledge this procedure has not been described previously. Other roentgenographic methods have proved very successful in the hands of a limited number of physicians skilled in their use, but probably the reason that no method has been universally adopted is because it requires either a special technic difficult to master or additional expensive equipment. The method proposed is a very simple one requiring but one x-ray exposure and will afford an accurate measurement of the true conjugate. Physical examination can usually be relied upon to furnish all the data necessary for the estimation of the outlet.

There are two factors essential:

1. An unquestionable demonstration on the film of the points to be measured.
2. A method of measuring the distance between these points, taking into consideration the distortion caused by the object-film distance.

The best means of demonstrating both the promontory of the sacrum and the posterior surface of the symphysis pubis is by a lateral projection on a properly exposed x-ray film. The promontory of the sacrum cannot be demonstrated nearly as well on an anteroposterior film, even by the stereoscopic method.

In searching for a method of measuring the distortion of the conjugate diameter, it occurred to me that by placing an accurately graduated, metal ruler in the same plane as the conjugate diameter of the pelvis, the distortion on the film of the conjugate diameter would be equal to the distortion of the metal ruler regardless of the distance of the tube or pelvis from the film.

The metal ruler used for the purpose described above is a piece of  $\frac{3}{4}$ -inch brass tubing on which have been cut, by a threading machine, eight threads to each inch. This can be made by any plumber or mechanic. Brass has proved to be the most satisfactory metal for this purpose.

## METHOD OF PROCEDURE

1. Attach the metal ruler to the patient's back with strips of adhesive so that it lies over the spinous processes of the lumbar spine and sacrum in an absolutely vertical position. The lower end of the ruler lies in the cleft between the buttocks.
2. Place the patient laterally on the Potter-Bucky diaphragm. Make an accurate lateral exposure of the lumbar spine and pelvis centering the tube over the greater trochanter of the femur. Special attention is paid to the posture of the patient so that a true lateral projection is obtained. One should be able to demonstrate on the film the promontory of the sacrum and the symphysis pubis.
3. On the film measure the distance between the promontory of the sacrum and the upper border of the posterior surface of the symphysis pubis.
4. Lay off this distance on the shadow of the metal ruler.



Fig. 1.

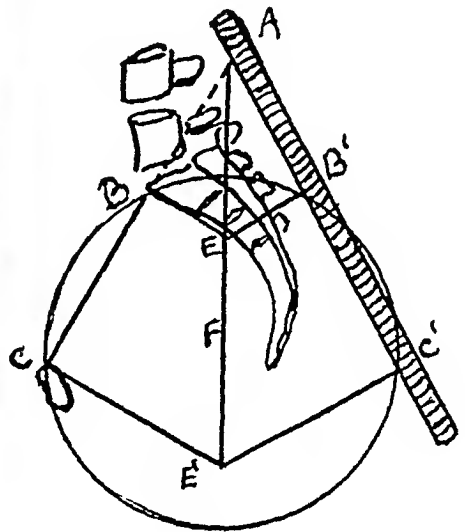


Fig. 2.

Fig. 1.—Illustrating the position of pelvis and ruler in this method of measuring the true conjugate diameter. (Dried specimen.)

Fig. 2.—Triangle  $AE'C'$  is congruent to triangle  $AEC$  since they are right triangles with hypotenuse and one angle equal. (Angle at  $A$ .) Similarly triangle  $AEB'$  and triangle  $AEB$  are equal. In congruent triangles, corresponding sides are equal. Therefore:  $AB'$  equals  $AB$ .  $AC'$  equals  $AC$  and, subtracting equals from equals,  $B'C'$  equals  $BC$ .

5. Count the number of notches included in this distance. Convert the number of notches into inches by dividing by 8, since each notch represents one-eighth of an inch. If desired, this measurement can be easily converted into centimeters. I intend to have a ruler constructed on which the graduations will be measured in centimeters.

To prove the accuracy of this method, I measured several metallic objects at various distances from the film. These measurements were invariably accurate. I have also measured the true conjugate diameter of several dried pelves and in each instance the roentgen measure-



ments corresponded exactly to those obtained by manual measurement of each pelvis.

This method has been applied very successfully in the Obstetrical Service at Morrisania City Hospital and I am now engaged in compil-

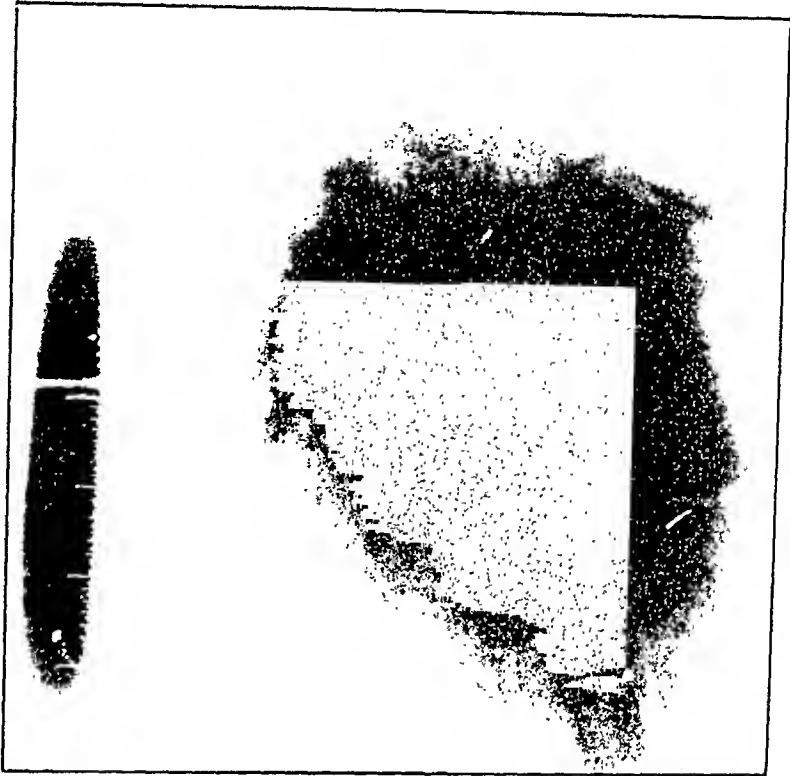


Fig. 3.—Showing roentgenogram of pelvis at beginning of labor, with ruler in position.

ing the data, obtained from a large group of cases, which will show the relation between measurement of the true conjugate and the history of the delivery.

I wish to express my thanks for the kind encouragement of Dr. Harry Aranow, Director of Obstetrics, and also wish to acknowledge the assistance of Dr. M. Friedman and Mr. Henry Aranow, Jr.

1882 GRAND CONCOURSE

---

Davidson, C. L.: Twisted Ovarian Cyst. A Procedure to Prevent Fatality From Embolism, *Am. J. Surg.* 27: 79, 1935.

It has not been an uncommon thing for an operation for twisted ovarian cyst to terminate fatally by cerebral embolism. If the twisted cyst is not disturbed, but is delivered into the abdominal wound and a hemostat is placed well below the last twist on the broad ligament, that is, beyond any discoloration or hemorrhagic areas in the pedicle, this procedure will tend to prevent embolic terminations. It is felt that untwisting the cyst before amputation allows stagnated blood to get into circulation and thus cause embolism.

J. THORNWELL WITHERSPOON.

# ABDOMINAL PREGNANCY WITH REMOVAL, AFTER EIGHTEEN YEARS, OF A SIX MONTHS' LITHOPEDION\*

ADRIAN W. VOEGELIN, M.D., PHILADELPHIA, PA.

THE case about to be reported presents some interesting features. Mrs. H. S., aged fifty-two, weight about 150 pounds, became ill on Aug. 16, 1934, with general aching and soreness over the lower part of the abdomen. The pain was not acute, did not radiate and was equal on the two sides. The bowels moved normally but her abdominal symptoms grew worse and two days later we ex-



Fig. 1.—Photograph of lithopedion.

amined her by request of the family physician. The patient by now had developed intense nausea but only occasional vomiting and was complaining of severe pains in the lower abdomen. She looked quite ill. Menses had begun at fourteen, were regular at thirty-day intervals. She first became pregnant at twenty-six years of age and had a spontaneous delivery. Subsequently, all of six pregnancies ended in abortions or miscarriages. Menopause occurred suddenly at forty-eight, and she had had no trouble since, except that she felt a lump in her abdomen when tired and lying on her back. Temperature was 100° F., pulse 100, and respiration 20.

\*Read at a meeting of the Obstetrical Society of Philadelphia, January 3, 1935.

On examination, the abdomen was moderately obese and slightly tympanitic. There was marked tenderness over all quadrants but particularly in the lower right quadrant. Spasm and rigidity were present over both lower quadrants most marked in the right groin. Vaginal examination caused much pain and was not conclusive. The cervix felt normal and was slightly movable with much pain. The uterus was not outlined. The right fornix felt fuller and more tender than the left. A tentative diagnosis of pelvic inflammatory disease or twisted ovarian cyst was made and the patient was sent to the Kensington Hospital for Women. Physical examination after admission was largely negative. Blood pressure was 120/80; heart sounds of fair quality. Hb was 80 per cent, R.B.C. was 4,050,000, W.B.C. was 15,250. The urine showed a heavy trace of albumin, a trace of



Fig. 2.—Roentgenogram of lithopedion showing curving of spine to aid compression into smallest space.

sugar and occasional light granular and hyaline casts. Wassermann, blood sugar, and urea tests later were normal.

The patient was given appropriate supportive treatment and on August 21, under avertin anesthesia, the abdomen was opened through a right rectus incision. A right tuboovarian abscess with many pelvic and omental adhesions, containing odorous pus and involving the appendix, was first found. The right tube and ovary and appendix were liberated and removed. The uterus was of average size and not much involved but the left tube and ovary could not be found, the cornual region being smooth and rounded. While palpating the left side, a large mass was found above the brim of the pelvis, lying free in the abdominal cavity except for its almost complete covering of omentum. As they were somewhat separate, the long bones with their sharp ends were first encountered and removed. Then the lithopedion itself was shelled out without much bleeding. There was no evidence of a placenta, membranes or a pelvic attachment. The ab-

domen was closed with drainage. Part of the wound became infected but the patient was discharged in good condition five weeks later.

On questioning this patient in detail we discovered that in 1916, when about five months pregnant she had visited our prenatal clinic when the fetal heart sounds were heard by several doctors. She then stopped coming, became quite large and in about two months had a "flooding spell." An outside doctor told her she was not pregnant. She lost considerable blood at home but after a few days in bed she quickly recovered. Her periods returned but with more pain than formerly. There were no further pregnancies and she had no severe illnesses.

But for this accidental discovery, she might have carried the stowaway for the rest of her life. Apparently at some time during this period, nutritional disturbances must have destroyed the left tube and ovary. The sex of the lithopedion was indeterminate. There was a thin coating of fatty material beneath which was the hard calcified fetal mass. A small quantity of odorless thick yellow fluid was drained from its interior. Based on Scammon and Calkins' work we calculated the age of this lithopedion to be at least six lunar months.

---

## CORPUS LUTEUM TUMOR

ORAN I. CUTLER, M.D., LOMA LINDA, CALIF.

*(From the Department of Pathology, College of Medical Evangelists)*

**D**URING the past few years much attention has been paid to the endocrine functions of certain ovarian tumors. In this relation, a tumor which has recently come to my attention is of considerable interest.

V. B., aged twenty-two, unmarried, began menstruating at the age of thirteen. Her periods were never regular. Frequently she went more than twenty-eight days between menses. Flow lasted five to seven days and was profuse. Of late the bleeding had become more prolonged and profuse, being present most of the time. Pelvic examination showed the uterus to be of normal size and in normal position. A small cervical erosion was present. The right adnexa were apparently normal. The left ovary was palpable and seemed enlarged.

During the twenty-five days following this examination, eight injections of 1 c.c. each of antuitrin-S were administered. This stopped the prolonged and excessive menstrual flow. Six and one-half months after the series of injections of antuitrin-S was completed, the patient again entered the hospital, this time for an appendectomy. During these six and one-half months the menstrual flow had been of ordinary duration and quantity. The last two periods had been more painful than former ones. The patient had also had two attacks of pain in the right lower abdominal quadrant not associated with the menses. Nausea and some vomiting were present with the pain. At operation a large appendix packed with fecaliths was found. The left ovary was also removed.

*Pathologist's Report.*—The left ovary consisted of a smooth, firm, oval mass which measured 3.5 by 4.5 by 6 cm. On the cut surface, a thin layer of white tissue, 1 to 3 mm. in thickness, was present at the periphery. This layer was very loosely adherent to an underlying mass which occupied most of the ovary. Much of this mass was composed of tissue which was bright yellow in color. Irregular areas in the center of the mass were white. Some of the white areas were firm and opaque. Others were soft and translucent.

The microscope showed that the peripheral white layer consisted of ovarian cortex

in which were fairly numerous immature follicles. The yellow tissue (Fig. 1) was composed of anastomosing strands and sheets of cells having oval nuclei and abundant cytoplasm. Fat stains demonstrated much lipoid material in the latter. The cells were of quite uniform morphology and mitoses were not seen. However, the folded arrangement of the sheets of cells found in the ordinary corpus luteum was not observed. There were fairly numerous small blood vessels ramifying among the strands of cells, but relatively little connective tissue was present. The white translucent areas of the tumor consisted of edematous connective tissue in which tumor cells were loosely scattered. The tumor cells in these areas possessed less cytoplasm than in the yellow areas and the cytoplasm contained relatively little lipoid. The firm white areas consisted of dense fibrous tissue in which some areas of tumor cells were buried (Fig. 2). The tumor cells in these areas contained very little lipoid.



Fig. 1.

Fig. 1.—Cellular lipoid rich portion of tumor near capsule.



Fig. 2.

Fig. 2.—Dense fibrous area with islands of cells.

#### DISCUSSION

Plate<sup>1</sup> has made the suggestion that granulosa cell tumors may become luteinized. He found an orange-sized tumor in a patient twenty-three years of age. Two years before the tumor was removed, the patient had a curettage for treatment of profuse menstruation. After the curettage the menses became irregular, followed by sudden cessation seven months before operation. The breasts were swollen and contained colostrum. After the operation the menses reappeared and the breasts returned to normal. Most of the tumor was yellowish and composed of strands and groups of more or less columnar cells containing lipoids. In areas the cells were smaller and fat poor. Plate states that two similar tumors have been seen by Lecene.

Benda and Krans<sup>2</sup> have recently reported the case of a woman thirty-eight years of age who had had amenorrhea for two years. At operation a solid ovarian tumor which presented yellow areas was found. Lipoid was present in the cytoplasm of the tumor cells. It seemed quite conclusive that this growth consisted of a granulosa cell tumor undergoing luteinization.

In the case which I have studied, profuse irregular menses were present, as in patients having granulosa cell tumors. The profuse bleeding ceased after the in-

jection of anterior pituitary-like hormone from urine produced during pregnancy. The production of a hormone (Collip<sup>3</sup>) by the anterior pituitary which causes the transformation of granulosa cells into those of a corpus luteum has been quite definitely demonstrated. It has further been shown that anterior pituitary-like hormone in urine during pregnancy causes only theca luteinization when acting alone. However, in the presence of the luteinizing hormone of the anterior pituitary the action of each is reinforced by the other. It would thus seem reasonable to believe that the change in the character of the menses of the patient under discussion was associated with the luteinization of the granulosa cell tumor. Amenorrhea had not yet appeared in this patient as it had in the cases of Plate and of Benda and Kraus.

## REFERENCES

- (1) Plate, W. P.: Arch. f. Gynäk. 153: 318, 1933. (2) Benda, and Kraus, E. J.: Arch. f. Gynäk. 157: 400, 1934. (3) Collip, J. B., Selye, H., Anderson, E. M., and Thomson, D. L.: J. A. M. A. 101: 1553, 1933.

## THE FACTOR OF BIRTH TRAUMA IN CANCER OF THE UTERINE CERVIX\*

CATHARINE MACFARLANE, M.D., F.A.C.S., PHILADELPHIA, PA.

(From the Department of Gynecology, Woman's Medical College of Pennsylvania)

IN A TIME of rapidly changing opinion, when the indivisible atom of our childhood has been split into many parts, when Newton's law no longer accounts for the falling apple and when the ovum no longer dominates menstruation, it becomes necessary to scrutinize carefully each familiar fact.

The fact to which I invite attention is the relative incidence of cancer of the uterine cervix in parous and in nulliparous women.

The literature on this subject was reviewed recently by Martzloff who concludes in the 1933 edition of Curtis' *Obstetrics and Gynecology* that "over 90 per cent of the cases of cancer of the cervix give a history of one or more previous pregnancies." Probably most of us are in the habit of making somewhat similar statements. Nevertheless these statements do not tell the whole story.

Last spring my own statistics were gently challenged by a physician who asked, "What is the relative frequency of parous and nulliparous women in your Hospital?" I was unable to answer this question, agreed that it was important and determined to rectify my ignorance at the earliest possible date.

As a result, I am able to present certain statistics based on the case histories of four thousand women admitted to the Gynecological Wards

\*Read at a meeting of the Obstetrical Society of Philadelphia, January 3, 1935.

of the Woman's Medical College Hospital and Woman's Hospital of Philadelphia. These statistics are shown in Table I.

TABLE I. INCIDENCE OF CANCER OF THE UTERUS IN 4,000 GYNECOLOGIC PATIENTS

NO. OF CASES	AGE	CA. OF CERVIX	CA. OF BODY	TOTAL CA. OF UTERUS
1,000 Single, white nulliparous	20-77	3 (3)* 6	20	26
1,000 Married, white nulliparous	20-79	7 (7)* 14	10	24
1,000 Married, white parous	20-79	37	9	46
1,000 Married, black parous	20-75	28 (14)* 42	1 (1)* 2	44

\*No microscopic examination.

From the standpoint of cancer of the cervix, the chief interest of this table lies in the second and third groups.

The second group comprises 1,000 married white women between twenty and seventy-nine years of age who have not borne children. Cancer of the cervix was found in fourteen of these patients or 1.4 per cent.

The third group comprises 1,000 married white women between twenty and seventy-nine years of age who have borne one or more children (deliveries at six months to full term were included). Cancer of the cervix was found in thirty-seven of these patients or 3.7 per cent.

Therefore, according to these statistics, cancer of the cervix occurs about three times as often in married white women who have borne children as in married white women who have not borne children.

In these two groups, the factor of intercourse, venereal infection and contraceptive measures were presumably the same. In the second group, two other factors must be considered. The first of these is stimulation of the cervical epithelium during pregnancy by anterior pituitary hormones (Hofbauer). The second factor is birth trauma.

The factor of pituitary stimulation of cervical epithelium, if, when and as it occurs, is quite beyond our control. The effects of birth trauma can be controlled.

We are all familiar with the appearance of the smooth, firm cervix of the primigravida. We are all familiar with the appearance of this cervix after a difficult labor: flabby, bleeding, torn to a greater or less degree. We are all familiar with the appearance of this cervix six months to a year after delivery.

If the tear has been slight, healing will be complete. If the tear has been extensive, pathology will be present. If the sphincter of the external os has been torn, the cervix will be thickened, its mucous membrane everted, infected, and inflamed.

In this area of chronic epithelial irritation, those puzzling microscopic lesions termed precancerous, canceroid, suggestive of cancer, early cancerous, are very frequently found. It seems worth while to attempt to prevent their formation by means of cervical repair.

The best time to repair the cervix would seem to be when the laceration occurs or within the first twenty-four hours after delivery.

Most authorities on obstetrics are opposed to the idea of primary repair, recommending it only for the control of hemorrhage from a torn cervical artery.

From the gynecologic point of view, laceration of the cervical sphincter is almost as important as laceration of the cervical artery. Neglect in one case will result in immediate death from hemorrhage. Neglect in the other case may result in eventual death from cancer of the cervix, a late maternal mortality.

Primary repair of the lacerated cervix is no more difficult and no more dangerous than primary repair of the lacerated perineum or primary repair of the episiotomy incision. All three procedures demand technical ability, aseptic equipment and adequate assistance.

#### CONCLUSIONS

1. Cancer of the cervix occurs about three times as often in married white women who have borne children as in married white women who have not borne children.

2. This increased frequency in the parous group is probably the result of birth trauma.

3. The after effects of birth trauma should be prevented by primary repair of the lacerated cervix.

701 MEDICAL ARTS BUILDING

---

Terada, E.: *Statistics of Uterine Cancer*, Japanese J. Obst. & Gynec. 16: 432, 1933.

Among 14,941 female patients seen at the Himeji Red Cross Hospital there were 355 cases of uterine cancer (2.38 per cent). The cervix was involved in 97.8 per cent. The youngest patient was 24 and the oldest 73, the average age for the cervical cancers being 47.4 years and for the corpus carcinomas 54.9 years. The parity was distributed as follows: nulliparas, 8 per cent in the cervix and 25 per cent in the corpus cases; primiparas, 4.6 per cent in the cervix and 12.5 per cent in the corpus cases; para ii to para iv, 4.6 per cent in the cervix and 12.5 per cent in the corpus cases; women with more than four children, 56.2 per cent in the cervix and 12.5 per cent in the corpus cases.

Cancer of the cervix occurred three times more frequently on the posterior lip than on the anterior. In 11 of the 355 cases, pregnancy was associated with the cancer of the uterus (3.2 per cent). The symptoms were as follows: watery discharge 34.7 per cent, bloody discharge 9.3 per cent, uterine hemorrhage 51.4 per cent and pain 13.2 per cent.

J. P. GREENHILL.



# TORSION OF THE PREGNANT UTERUS IN PATIENTS WITH KYPHOTIC PELVIS\*

BENJAMIN RABINER, M.D., F.A.C.S., BROOKLYN, N. Y.

(From the Beth Moses Hospital)

A SURVEY of the current textbooks on obstetrics discloses that the complication of torsion of the pregnant uterus is mentioned briefly or not considered at all. Most of the cases of torsion of the pregnant uterus reported in the literature were associated with tumors of the uterus, ovarian cysts, bicornuate uterus, or some form of asymmetry of the uterus. Two cases in which there was no pathology of the uterus or adnexa were reported by Egon Wienzierl. One was in a patient with sinistroseoliosis of the spinal column and both cases were discovered during the performance of cesarean sections, performed in the interest of mother and child rather than for shock and hemorrhage. One case showed ninety degrees and the other, two hundred degrees of rotation of the uterus, and neither was diagnosed prior to operation. Appended herewith is the report of a case of ninety degrees torsion of the pregnant uterus in a patient with a kyphotic pelvis.

Mrs. M. H., aged twenty-three, Italian, married eleven months, nullipara, gravida i. Her last period occurred July 8, 1933, and the estimated date of confinement was April 15, 1934. Patient had had a caries of the spine at two and one-half years.

*Physical Examination.*—Sept. 6, 1933, height: 4 feet 1 inch; weight: 93 pounds, with a marked lower lumbar kyphosis. Vaginal examination: Pregnant uterus about seven weeks was found. Pelvic measurements were as follows:

I.C.	28	R.O.	20.5	D.C.	11
I.S.	25	L.O.	20.0	Bisischial	5.5-6
I.T.	27	E.C.	16.5		

The symphysis was prominent and pubic arch narrow.

The antepartum course was essentially normal except for vomiting in the early months of pregnancy, which was easily controlled. The patient's weight increased from 93 pounds to 110 pounds. After the first half of pregnancy, the abdomen was pendulous. The fetal parts were easily outlined; more so than usual. The fetal heart could be heard only over the xiphoid cartilage. As the pregnancy advanced to term, the abdomen became so pendulous that the fetus appeared to be in a sac hanging over the symphysis, especially when the patient was erect. The umbilicus could not be seen after the fifth month and was located on the posterior surface of the pendulous sac. The abdominal wall was extremely thin, stretched, and under tension. The abdominal veins were prominent and distended.

X-ray examination, March 20, 1934, showed marked lumbar kyphosis due to destruction of the bodies of the third and fourth lumbar vertebrae; a well-developed fetus in the false pelvis in the transverse position with the head in the right iliac fossa. The transverse diameter of the outlet was contracted, with marked narrowing of the bisischial diameter.

On April 10, 1934, five days prior to the estimated date of confinement, an elective cesarean section was performed under local infiltration anesthesia (1 per cent

\*Read before the Brooklyn Gynecological Society, March 1, 1935.

novocaine). The abdominal wall was infiltrated in layers. The skin, fascia, and muscle were under tension and of extraordinary thinness. In order to make a sub-umbilical midline incision, it was necessary for the assistant to raise and hold the pendulous sac upward and cephalad, both during infiltration and incision. When the abdomen was opened, the uterus appeared markedly cyanotic and congested, and the uterine veins were full and prominent. The right tube and ovary presented to the left of the midline incision; the left tube and ovary were in the hollow of the sacrum and to the right. The uterus was rotated approximately ninety degrees from right to left. The tubes and ovaries appeared congested and edematous. The uterus was rotated to its normal position following which the cyanosis and congestion markedly subsided. A low midfundal incision was made and the baby, lying in the right scapuloposterior position, was extracted by the feet. The placenta was on the anterior wall of the uterus and was extracted manually. An ampule each of pituitrin and gynergen was given hypodermatically at the time of the uterine incision. Bleeding seemed more profuse than usual. The uterus contracted firmly. The uterus was closed in two layers, one deep and one superficial of chromic No. 2 interrupted sutures, and peritonealized with a running "baseball stitch" of No. 2 plain catgut. The tubes were infiltrated and sterilization was performed by the Pomeroy method. The abdomen was closed in layers. The patient made an uneventful recovery and was discharged with a living baby (baby's birth weight 5 pounds 14 ounces), twelve days after operation.

The follow-up showed a firm abdominal wall, no postoperative hernia, well-involved uterus, cervix backward, fundus forward, and nonadherent; adnexa and parametrium negative.

#### REFERENCE

Wienzierl, Egon: Monatschr. f. Geburtsh. u. Gynäk. 59: 29, 1922.

358 NEW YORK AVENUE

---

## SQUAMOUS CELL CARCINOMA OF CERVIX; ADENOCARCINOMA OF FUNDUS OF UTERUS\*

MARK T. GOLDSTINE, M.D., CHICAGO, ILL.

MRS. L. W., aged forty-six years, married twenty-three years; one child aged eighteen; no miscarriages. Nothing remarkable in family history. Menstruation began at fifteen, irregular, usually coming on the average of every six weeks; flow scant, never lasting more than two days. Menstruation ceased at about age of thirty-three, and there were no periods or bleeding for twelve years previous to two months before examination. At this time there appeared a very little spotting of blood, which increased in amount and showed every day. Bleeding started simultaneously with a very severe attack of herpes on head and neck. Weight at the time of examination 225 pounds. Patient has always been quite heavy and had no recent loss of weight.

*Pelvic Examination.*—Vulva and vagina showed no pathologic changes. The cervix was large, with several small stellate lacerations; on the posterior lip of the external os and well away from the opening was a raised area 1.5 c.c. in diameter, dark red in appearance and not bleeding, and firm to touch. The body of the uterus was the size of an eight weeks' pregnancy, smooth and firm,

---

\*Presented before the Chicago Gynecological Society, January 18, 1935.

and the uterus was easily movable. Appendages were apparently normal. The nodule on the posterior lip of the cervix was completely excised, a curettement was done, and we obtained a large amount of soft friable material from a pocket in the left horn of the uterus. The cavity of the uterus was about 15 cm. in length.

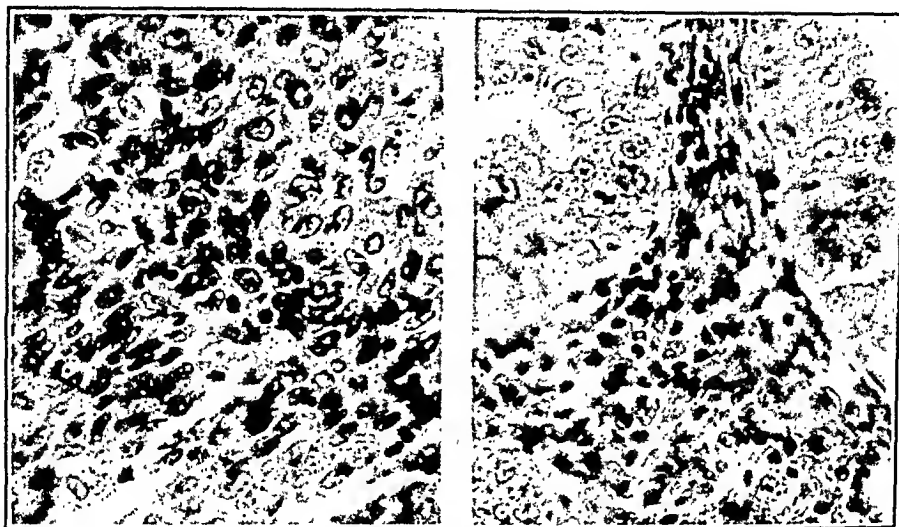


Fig. 1.

Fig. 2.

Fig. 1.—High power of section showing squamous cell carcinoma of cervix.

Fig. 2.—High power of adenocarcinoma of the fundus of uterus.



Fig. 3.—Microphotograph showing both squamous cell carcinoma A, of cervix and adenocarcinoma of fundus B.

Microscopic examination showed the nodule from the cervix to be a distinct squamous cell carcinoma (Fig. 1). The tissue from the fundus was typical adenocarcinoma (Fig. 2).

Hysterectomy was performed one week later with the removal of a large symmetrical uterus previously described. The fundus contained a large amount of friable tissue which was adenocarcinoma.

Microscopic study showed no carcinoma in the lower uterine segment. There was approximately 8 cm. distance between the carcinoma of the fundus and that of the cervix (Fig. 3). There was no evidence of more carcinoma in the cervix,

and we apparently removed all in the original biopsy. There was a mild chronic cervicitis. There was congenital absence of one ovary. The wall of the uterus was 3.5 cm. in thickness, firm but not hard and appeared to have more fibrous content than usual. The carcinoma invaded the wall to an average depth of 1 cm. There were no metastases found.

---

## FULL-TERM UNILATERAL TUBAL TWIN PREGNANCY

JOHN A. FERGUSON, M.Sc., M.D., AND ISRAEL S. OTIS, M.D., F.A.C.S.,  
MERIDEN, CONN.

*(From the Departments of Pathology and Surgery of The Meriden Hospital.)*

UNILATERAL tubal twin pregnancy is not common. A number of authentic cases, however, have been reported. Arey in 1923 collected from the literature thirty-eight cases which he accepted as authentic, and added two cases of his own. We have found reports of three cases of unilateral tubal twin pregnancy which have been published since 1923. Kynock reported a case in 1924, Nota in 1929, and Deichgraber reported a case in 1931 in which the fetuses were in the sixth month of development. In Folet's case, listed by Arey, one of the fetuses reached maturity.

We present an additional case of unilateral tubal twin pregnancy which we believe is unique, in that both fetuses reached maturity and were apparently alive at full term, though they were delivered dead by abdominal section at the twelfth month. We were unable to find a similar case described.

Patient was a German woman thirty-two years of age. Two children alive and well, delivery normal in each instance. Menstrual periods always regular. Patient had for the last four years a chronic cervicitis which was due to the gonococcus.

The last menstrual period ceased on Nov. 20, 1925, and was followed by morning sickness, nausea and vomiting. The patient thought at this time that she was pregnant. Her former pregnancies began exactly the same way.

On March 3, 1926, patient was admitted to the hospital complaining of left lower quadrant abdominal pain and vaginal bleeding. She stated that about one month prior to this admission she had backache and abdominal cramps at irregular periods. The symptoms disappeared after nineteen days in the hospital, and the patient was discharged with a tentative diagnosis of chronic salpingitis or ectopic pregnancy.

The patient stated that she felt definite fetal movements on June, 1926, which was about seven months after the cessation of the menses. The abdomen was considerably enlarged at this time.

On September 15, over nine months after the last menstrual period, the patient was admitted to the hospital with the complaint of slight vaginal bleeding. She thought that she was at full term and that labor ought to begin. No fetal heart sounds were heard. After five days in the hospital bleeding ceased and the patient was again discharged.

On November 16, or about twelve months after cessation of the last menstrual period, patient was admitted to the hospital for the third time. This time she complained of weakness, fatigue, and loss of weight. On physical examination no fetal heart sounds were heard. (Bimanual examination at this time revealed a small, firm uterus which was quite easily outlined.) Palpation revealed definite fetal parts and laparotomy was decided upon.

*Laparotomy.*—The abdomen was opened by a long incision just to the left of the midline. There was a large mass in the left side of the abdomen which was covered over with omentum and coils of small intestine. The mass appeared to be attached to the left tube, and the uterus was pushed to the right side of the abdomen. The mass was freed and delivered through the abdomen. At this stage of the operation, the wall of the mass ruptured and two dead female fetuses were removed from the sac. The sac appeared to be adherent to the left side of the uterus so a subtotal hysterectomy was performed. The abdomen was closed without drainage. The patient made an uneventful recovery and is alive and well at the present time.

*Pathologic Examination.*—The specimen consisted of two well-developed similar female fetuses, uterus with right tube and ovary attached, and placenta with a large firm membranous sac situated in the region of the left tube and ovary.



Fig. 1.



Fig. 2.

Fig. 1.—Shows normal uterus with right tube and ovary attached. A portion of cervix and the internal os are shown. The isthmus of the left tube is shown and also the inferior surface of the placental mass.

Fig. 2.—Shows the fetuses.

One twin measured 40 cm. and weighed 1,730 gm. The other measured 34 cm. and weighed 1,400 gm. The skin over each was firm and smooth and was covered with an abundant vernix caseosa.

The mass to the left of the uterus measured 14 by 8 cm. and was composed of placental tissue. The external surface was covered by whitish glistening fibrous tissue which extended beyond the edge of the placental mass and formed the outer layer of the sac. Two cords were implanted into the placental mass about 7 cm. apart. There was one chorion and two amnions. The twins were apparently uniovular. The left tube was identified at the left margin of the uterus. It then appeared to fade out over the placental mass. The left side of the uterus was slightly adherent to the placental mass but the adhesions were readily broken down.

The myometrium was 2.5 cm. in thickness. The endometrium was pinkish and smooth. The right tube 7.5 cm. in length and appeared normal. The right ovary measured 3.5 by 2 cm. and contained two reddish corpus luteum cysts.

*Microscopic Examination.*—Sections were taken from the placenta and membranes, the right tube and ovary, both cords, and from the isthmus of the left tube. The tissue was fixed in 10 per cent formalin and routine H & E stains were made. Right tube and ovary, uterus, isthmus of left tube, and cords appeared normal.

*Placenta:* The cells of the placenta did not stain clearly. There were a number of small foci of calcification and a few of the blood vessels were thrombosed. The outermost layer of the placenta was composed of fibrous tissue. This layer of fibrous tissue also formed the outer layer of the membranes which enclosed the fetuses.

We have found reports of three cases of unilateral tubal twin pregnancy that have been published since 1923.

We believe that the death of the fetuses in the case described was probably due to mechanical interference with their blood supply as a result of the pressure of the fetuses on the placental blood vessels. It seems reasonable to expect that had the diagnosis been made and laparotomy performed at the ninth month instead of the twelfth, viable fetuses would have been recovered.

Including the case described above, a total of forty-four proved cases of unilateral tubal twin pregnancies has been published up to 1933.

#### REFERENCES

*Arey, Leslie B.:* Surg. Gynec. Obst. 36: 407, 1923. *Kynock, J. R.:* Edinburgh M. J. 31: 332, 1924. *Nota, F.:* Rassegna d'ostet. e ginee. 38: 816, 1929. *Detthgraber, H.:* Zentralbl. f. Gynäk. 55: 611, 1931. *Folet:* Ann. di ostet. 45: 190, 1896.

## A NEW INSTRUMENT FOR THE ACCURATE READING OF THE MEASUREMENT OF THE DIAGONAL CONJUGATE

R. GORDON DOUGLAS, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell Medical College)

NO INSTRUMENT has yet been devised which is satisfactory for the routine measurement of the diagonal conjugate from which the true conjugate can be estimated. The usual method employed consists in palpating the promontory of the sacrum with the tip of the second finger and while keeping the finger closely applied to its most prominent surface the radial side of the index finger or hand is closely applied to the pubic arch and this point marked by the index finger of the other hand. The hand is then withdrawn from the vagina and the distance between the tip of the second finger and the marked point is measured by an *assistant* using a Martin's pelvimeter, or some other caliper.

Variations in measurements obtained by senior members of our attending staff upon the same patient led to an investigation of the method employed. Much to our surprise it was found that the pelvimeters in use in the clinic which were relatively new instruments thought to be the best procurable, varied as much as one-half a centimeter on either side of a given mark so that an accurately palpated diagonal conjugate measurement for instance could be interpreted as varying from 11.5 cm. to 10.5 cm. depending on the instrument used for measuring the distance. The instruments were sent back to the manufacturer for correction but later after routine use the differences were again found. The variation so found is not important in external pelvimetry but an error of as much as 1 cm. in the measurement of the diagonal conjugate may lead to a serious error in judgment in deciding on the treatment of a patient.

The instrument shown in Fig. 1 was gradually evolved in this hospital and it has been in use in all examining rooms in our Out-Patient Department, the examining rooms on our various pavilions, and in all our delivery rooms, for the past two years. In addition, practically all members of our attending staff now use the instrument in their private offices. It consists of a single piece of monel metal, 2 mm. thick, angulated at right angles so that there is a base 6 cm. square with screw holes to attach the instrument permanently to the wall, preferably on the tiling over a washstand. The portion of the instrument projecting from the wall is 14 cm. in length, 2.5 cm. wide, and is graduated in quarter centimeters from 8 to 13 cm. from the base. The method of employing the instrument is simple and illustrated in Fig. 1.

The advantages of using this device for measuring the distance of the diagonal conjugate marked on the hand are:

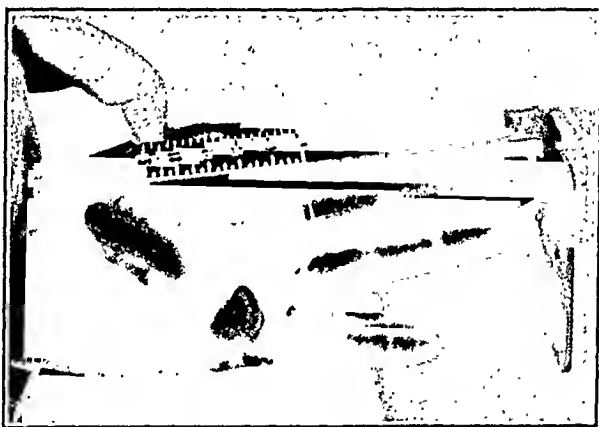


Fig. 1.

1. The measurement so recorded can be accurately read on the scale with no possibility of a variation from the correct reading, thus eliminating an unknown possible error that may develop in a movable instrument after varying periods of use.

2. The procedure is carried out entirely by the operator. The assistance and possible errors of a second person operating a pelvimeter are thus eliminated.

3. The same pressure can be exerted by the second finger on the base of the instrument as was exerted on the promontory of the sacrum.

4. The instrument is simple, inexpensive, will not deteriorate and should last indefinitely.

5. It requires no upkeep except cleaning which is a very simple process.

The original instruments in use in the Woman's Clinic of the New York Hospital, were handmade by the engineering department of the Hospital and have proved entirely satisfactory.

This appliance is made by the G. P. Pilling & Son Company, Philadelphia.

# SARCOMA AND ADENOCARCINOMA OF BODY OF UTERUS; ADENOCARCINOMA OF CERVIX\*

MARK T. GOLDSTINE, M.D., CHICAGO, ILL.

MRS. H. R., aged fifty years; married thirty years; two children, youngest twenty-four years; no miscarriages. Both parents dead several years from cardiovascular disease. One sister died at the age of forty-two from carcinoma of the breast; one sister living and well. Menstruation began at about thirteen years, regular, thirty-day type, and ceased at forty-seven. No blood was seen for two years. A very small discharge of blood from the vagina appeared one year previous to observation, increasing in amount until for two months it was a

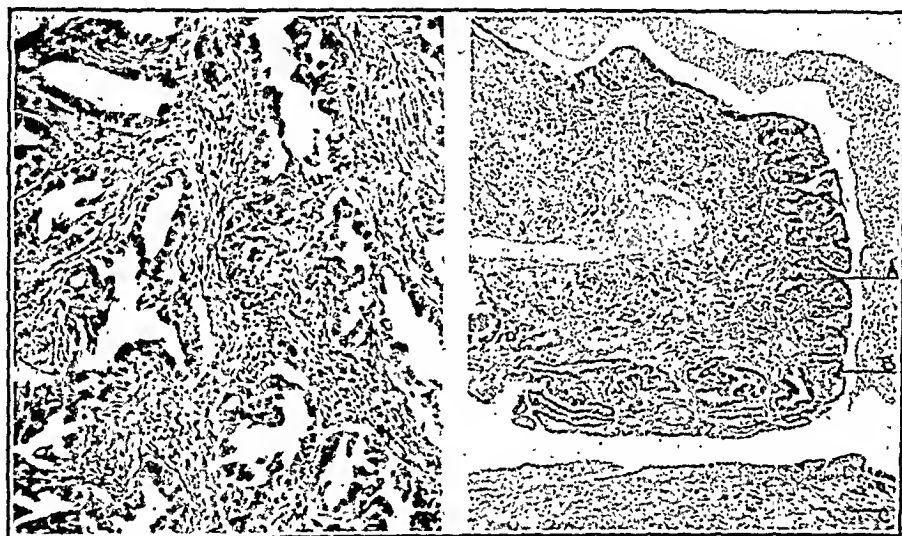


Fig. 1.

Fig. 2.

Fig. 1.—Photomicrograph showing adenocarcinoma of cervix.

Fig. 2.—Photograph showing sarcoma in the body of the uterus and the adenocarcinoma B, along the edge. The adenocarcinoma of the cervix is shown in C.

daily occurrence though she never had a profuse hemorrhage. There was no evident loss of weight or extraordinary fatigue. Weight was 184 pounds. History otherwise not remarkable.

*Pelvic Examination.*—Patient was bleeding rather freely. Vulva and vagina showed no pathologic changes. Cervix somewhat larger than normal; external os freely patent with blood flowing from it. Uterus was the size of a six weeks' pregnancy, smooth, very firm, tender to touch, and anteverted and only very slightly movable. The appendages were apparently normal. There were some thickening and induration at the cervicovaginal junction in both broad ligaments.

A biopsy of the cervix and a curettage were done. There was a marked excavation in the cervical canal from which tissue was removed by splitting the cervix laterally on both sides. A large amount of tissue was removed with curette, and from upper right horn of uterus several fair-sized polypi. All tissue was very friable.

\*Presented before the Chicago Gynecological Society, January 18, 1935.



*Microscopically*, the tissue from the cervix was adenocarcinoma (Fig. 1), and the polyps were definitely sarcoma (Figs. 2 and 3).

Hysterectomy was performed and on opening the uterus there were two large masses protruding from the fundus covered by a markedly thickened endometrium. Microscopically these tumor masses were large, round and spindle cell sarcomas with numerous giant cells. The endometrial covering was typical adenocarcinoma (Figs. 2, 3, and 4). The myometrium was free from sarcoma,



Fig. 3.

Fig. 4.

Fig. 3.—Higher magnification of the same.

Fig. 4.—Higher magnification showing sarcoma A, and carcinoma, in body of uterus B.

and we cannot say that the adenocarcinoma of the cervix was an independent growth from the carcinoma of the body of the uterus (Fig. 4). At least from study of the uterus the epithelium and glands of the cervix were so much destroyed that a differentiation could not be made. The sarcomatous process was fairly early, because it had not invaded the myometrium and antedated the carcinoma, particularly in the polypoid tumors.

---

Preissecker, Ernst: The Use of the Colposcope in Gynecology, Zentralbl. f. Gynäk. 56: 2280, 1932.

The principal advantage of the colposcope lies in the ease of early diagnosis of carcinoma of the portio and cervix. Lesions on the posterior vaginal wall and fornix lend themselves especially well to inspection. For example, a lesion 1 mm. in diameter, thought to be leucoplakia, was shown to be an early carcinoma. Such a lesion might easily have been missed by the naked eye. Pregnancy may also be diagnosed by the third or fourth month. The fine subsurface vessels become much broader and more reticulated in pregnancy.

Squamous and columnar epithelium are readily differentiated, thus making the colposcope especially useful in distinguishing erosions due to infection, from "physiologic" ectropion.

The author concludes that the investigation of leucoplakic spots so as to establish an early diagnosis of carcinoma, is the most important function of the colposcope.

WILLIAM F. MENGERT.

## NONPOLYPOID SARCOMA OF CERVIX UTERI\*

MARK T. GOLDSTINE, M.D., CHICAGO, ILL.

MRS. M. B., aged forty-six, of Armenian nativity, married twenty-five years. She had had no pregnancies. Her entire immediate family were killed during the World War. Menstruation began at fourteen, regular twenty-eight-day type, and apparently normal as to duration and length. The first deviation from normal occurred at the regular menstrual period in August, 1934; it was very profuse and lasted about ten days instead of five. Two weeks later she had rather profuse bleeding for two days, and from then on bled more or less every day until about the middle of October, 1934, when she began to have daily

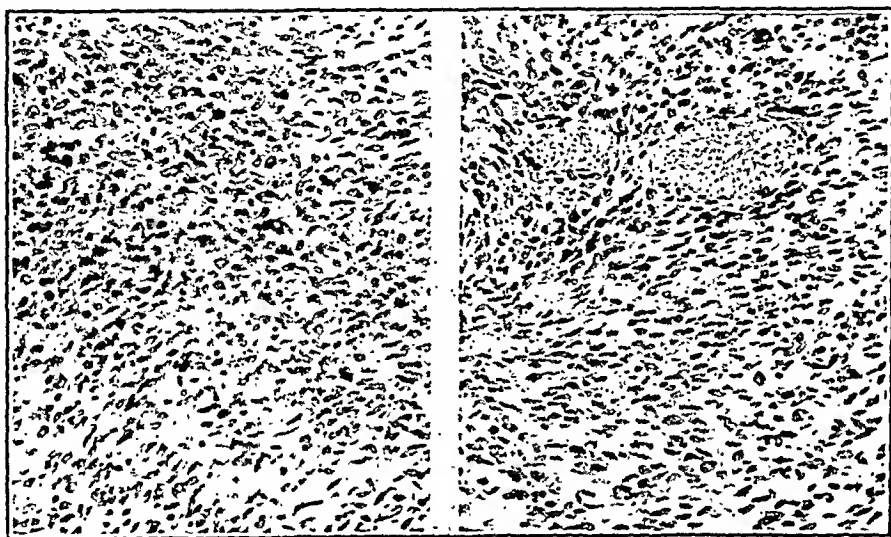


Fig. 1.

Fig. 2.

Fig. 1.—Section showing nonpolypoid sarcoma of cervix.

Fig. 2.—Another view of Fig. 1.

hemorrhages. On November 5, when she came for examination she showed all the objective signs of a rather severe secondary anemia.

*Pelvic examination* showed a negative vulva and vaginal canal. There was profuse bleeding from a large friable mass of tissue in the cervix. The external os was 3 cm. in diameter, the canal was obliterated, leaving only a shell of cervix, and only after removing a large amount of tissue were we able to find the opening at the internal os and reach the fundus of the uterus. The fundus was of normal size. The entire uterus was fixed, and there was very marked infiltration into the broad ligaments and rectovaginal septum. The appendages were apparently normal. Careful examination of the growth failed to reveal any polypoid formation, and we are fairly certain that this was not originally a polyp which had undergone tissue change. The growth infiltrated all the cervical tissue equally in its entire circumference. The fundus was curetted and a very small amount of tissue obtained.

\*Presented before the Chicago Gynecological Society, January 18, 1935.

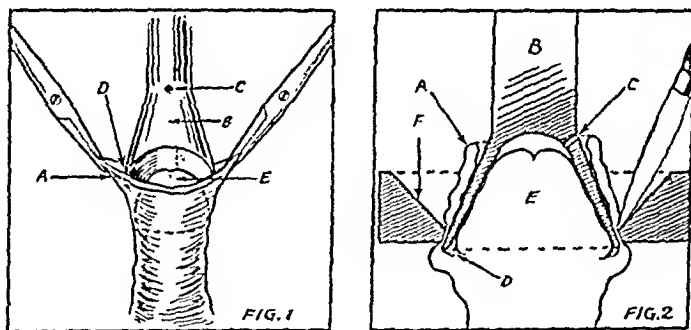
*Microscopic Examination.*—Sections through numerous pieces of tissue from the cervix (Figs. 1 and 2) showed a very irregularly growing malignancy. The cells had sizes from small to large, shapes from spindle to round, and nuclei which present many mitoses. These nuclei were fairly dark, round to oval, vesiculated, but did not contain nucleoli. The predominating type of cell was spindle in shape. There were no cell groups typical of carcinoma, no pearl formation. These cells were undoubtedly an undifferentiated sarcoma, which seemed to be very rapidly growing. A few cervical mucosal glands were present in two of the fragments of tissue. The endometrium was very atrophic and showed no evidence of malignancy.

The pathologic diagnosis was spindle cell sarcoma, in places undifferentiated.

## BLOODLESS CIRCUMCISION OF THE NEWBORN

HIRAM S. YELLEN, M.D., BUFFALO, N. Y.

**C**IRCUMCISION is one of the oldest operations recorded in the history of medicine, and while the method of procedure has kept pace with medical progress in general, there has always been the possibility of a hemorrhage with each case. Medical literature records many fatal hemorrhages and many infections as a result of circumcision of the newborn, and it is known that 2 per cent of all skin cancers are penis cancers. With this in mind we set about to develop a safe and



simple apparatus for the performance of this operation, with the result that we now have a clamp which not only eliminates the possibility of hemorrhage but also restricts the minimum chance of infection without the use of sutures.

About a year ago Aaron Goldstein of this city developed a clamp which we have used in many cases. This efficient instrument is small, compact, light as strength will permit, and can be operated without an assistant. The technic is quite simple, and the time required is less than that by any other method. With the use of this clamp we never employ sutures, no bleeding is encountered, and it leaves a clean-cut incision which heals perfectly in thirty-six hours with practically no chance of infection because the mucous membrane and skin are securely clamped together.

Fig. 3 is the clamp itself and Fig. 1 and Fig. 2 are diagrams showing the procedure. The following instruments and material are all that is really required: the clamp, 2 small hemostats, a probe with flattened end, a scissor with one blunt blade, an abscess knife or sharp-pointed scalpel (No. 12 Bard-Parker blade is ideal), sterile vaseline, and vaseline gauze.

## METHOD

After properly cleansing the penis (*E*) and pubis, the dorsal aspect of the prepuce (*A*) is put on a stretch by grasping it on either side of the median line with a pair of hemostats. A flat probe, anointed with vaseline, is then inserted between the prepuce and the glans to separate adherent mucous membrane. The prepuce is then gently drawn backward exposing the entire glans penis (*E*). This is again cleaned. In cases where the prepuce is drawn tightly over the glans, a partial dorsal slit will facilitate applying the cone of draw stud over the glans. (Note: If too long a slit is made, the cone has a tendency to slip off the glans. The slit should, therefore, be made only sufficiently long to enable the cone to be easily applied.) After anointing the inside of the cone (*B*), it is placed over the glans penis allowing enough of the mucous membrane to fit below the cone so that too much is not removed. The prepuce is then pulled through and above the bevel hole in the platform (*F*) and clamped in place. In this way the prepuce is crushed against the

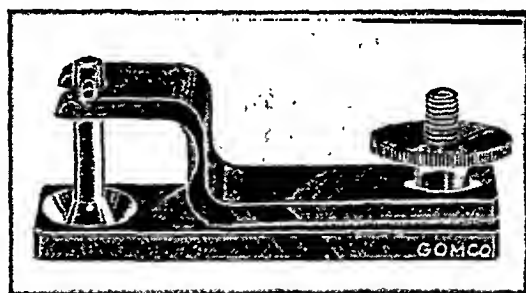


Fig. 3.

cone causing hemostases. We allow this pressure to remain five minutes, and in older children slightly longer. The excess of the prepuce is then cut with a sharp knife without any danger of cutting the glans, which is always protected by the cone portion of the instrument, leaving a very fine  $1/32$  of an inch ribbon-like membrane formed between the new union of the skin and mucous membrane. The pressure is then released. The circumcision is completed and the penis covered with vaseline gauze. No anesthesia is used.

On children older than twelve months, we find it is advisable to insert a few sutures.

At this date we have performed more than five hundred circumcisions on the newborn and as yet have not encountered any infection or hemorrhage.

---

Nelson, Warren O.: Studies of the Physiology of Lactation, Endocrinology 18: 33, 1934.

Ovarian hormones are active in the production of mammary gland growth during pregnancy, but they inhibit lactation during that period. In animals the high content of the ovarian hormones also appears to inhibit the secretion of the lactation-inducing hormone of the anterior hypophysis. With the decline in the ovarian hormone content at parturition the inhibitory influences are removed, the lactation-inducing hormone is secreted, and lactation results.

J. THORNWELL WITHERSPOON.

## A NEW COLPOSCOPE\*

HARRY O. MARYAN, M.D., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, University of Illinois)*

THIS colposcope is a monocular achromatic prismatic telescope giving magnifications of 6, 10, 13, 18, 25, and 30 diameters, at a focal distance of  $6\frac{3}{4}$  inches from the cervix to the front lens. It gives an erect image and has a fixed focus. It can be used on a circuit of 110 V. 60 Cy. A.C. or D.C. current, as it contains a rheostatic cord attached to the lamp.

The magnification can be increased by interchanging the eyepieces as they are numerically marked. The free working distance from the cervix to the front lens is  $6\frac{3}{4}$  inches. The distance from the introitus to the front lens is  $2\frac{3}{4}$  inches, leaving adequate room to perform direct biopsies, electrical cauterization, or coagulation, and to perform any manipulation which may be necessary, including Schiller's test. We have found for preliminary study that the six power magnification acquaints the observer with the general picture. After this preliminary study the ten power eyepiece is used to locate carefully the suspicious lesion or area. The ten power magnification is universally accepted by most observers. The higher the magnification the greater is the distortion and the smaller becomes the visual field.

The lamp is housed on top of the colposcope and just in front of the lens, with which it is in direct focus. It contains a 16 volt, 15 C.P. bulb. Proper illumination is very essential in order to give a nonglaring and a nonfogged field better to visualize the cervical lesion. The illuminating system, which contains a special condensing lens, gives a bright nondiffusing concentrated white oval light 50 mm. in diameter. We have found that by tilting the colposcope at an angle of  $30^\circ$ , and a little above the center of the speculum, we can get a better perspective. The colposcope is mounted on a rack and pinion, for finer focusing. And this in turn rests on the ball and socket joint with which one can angulate in almost any direction. To this is attached a short mounting sleeve, which fits into the adjustable tripod stand.

The next important step is to obtain adequate exposure and to have the field as dry as possible. For this we have used sand-blasted Grave's specula and Guttman's operative speculum. In this way unnecessary glare and reflections will be done away with, and will prevent the fogging of the colposcopic picture. We have found that Guttman's operative speculum is especially adapted for adequate vaginal exposure. The vagina, fornices and the cervix should be carefully wiped clean and dry with 1 per cent Lysol solution on a cotton sponge. The heavy mucoid discharge from the cervical canal may be dissolved with "caroid powder" on cotton applicator. It may be necessary to repeat this procedure several times to secure a dry field and avoid the fogging of the colposcopic picture. The observer can now visualize through the colposcope the cervix, the fornices, and the cervical canal and detect conditions that he was not able to see with the naked eye.

It seems to me that fundamentally, in order to interpret the colposcopic findings, one must be acquainted with the underlying pathology of chronic cervicitis. This we have shown in our clinic to be a deep infection of the compound racemose glands, which is characterized by a periglandular and a perivascular lymphocytic infiltration and a downward proliferation to the stroma and to the cervical lips of

\*Presented at a meeting of the Chicago Gynecological Society, October 10, 1934.

the compound racemose glands. This is what is generally termed as an erosion, but is a misnomer. Rightfully, it should be called a chronic pancervicitis or chronic cervicitis. It is this picture and the peculiarities that it gives which one has to understand before colposcopic findings can be correctly interpreted. This will enable the observer to differentiate between apparently normal and doubtful tissue.

The colposcopic findings should always be checked by multiple or serial tissue sections, and in this way mistaken tissue biopsies will be greatly reduced.

A malignant leucoplakia, shown in Fig. 2, presents a definite demarcation of

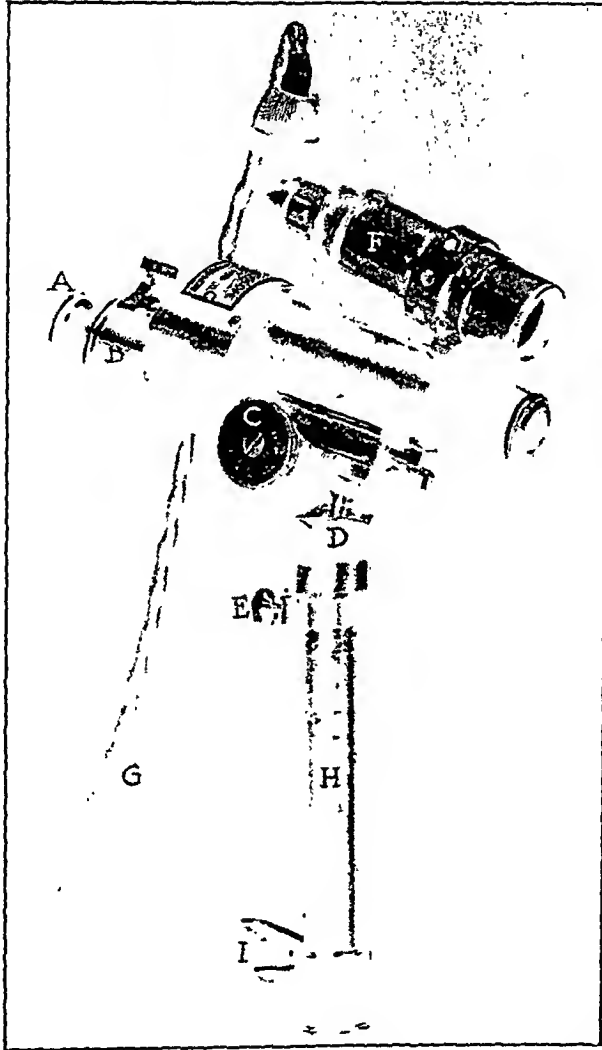


Fig. 1.—A, Eyepiece, B, telescope, C, micrometer, D, universal swivel joint, E, clamp of extension rod for telescope, F, lamp attachment, G, rheostatic cord, H, extension rod, and I, clamp of stand.

the normal from the malignant epithelium by means of the oblique line. This obliquity is characteristic and results according to Schiller from the more rapid growth of the deep layer of the carcinomatous lesion. The marked anaplasia of the cells, the hyperchromatosis, abundant mitoses, and the opaqueness of the staining quality of the cellular structures are also well marked. However, the basal membrane is intact. This picture of malignant leucoplakia, we feel, is diagnostic of incipient intraepithelial epithelioma.

In Fig. 2 is shown a marked hyperplasia and thickening of the stratified epithelium of the cervical lip surrounding the misplaced compound racemose glands in

the stroma of the portiovaginalis. Apparently the source of irritation is an infection of the compound racemose glands.

Colposcopy is primarily used for the detection of pinpoint leucoplakias, intra-

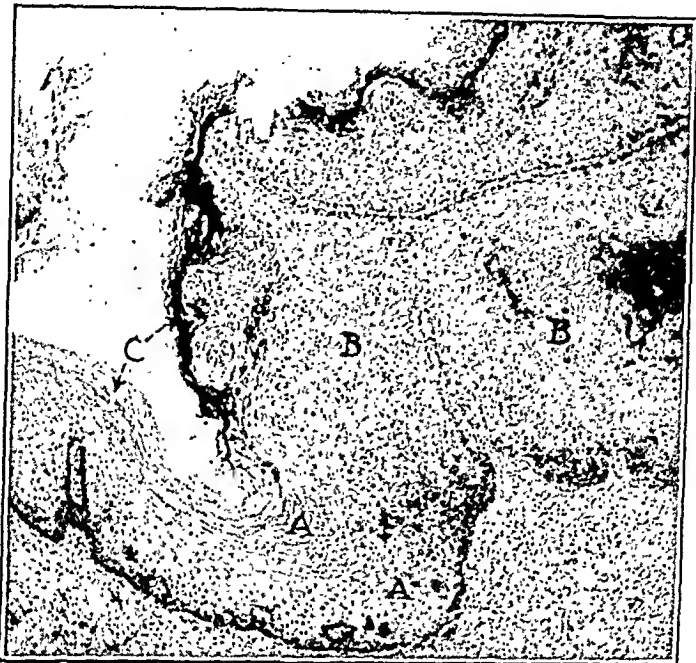


Fig. 2.—A, Oblique line, demarcating the normal from the malignant epithelium. B, Hyperplasia, hyperchromatosis, mitosis, and anaplasia of cells with intact basement membrane. C, Hyperkeratosis.



Fig. 3.—A, Marked hyperplasia and thickening of the stratified squamous epithelium. B, Misplaced compound racemose glands in stroma of portio vaginalis. C, Hyperplastic connective tissue.

epithelial epitheliomas, and to eradicate any suspicious cervical lesions. In this way the mortality incidence of 85 per cent of the hopeless cases of carcinoma of the cervix will be greatly reduced.

#### REFERENCE

- (1) Maryan, H. O.: AM. J. OBST. & GYNEC. 23: 555, 1932.

# Society Transactions

---

## OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF JANUARY 3, 1935*

The following papers were presented:

**Abdominal Pregnancy With Removal, After Eighteen Years, of a Six Months' Lithopedion.** Dr. Adrian W. Voegelin. (For original article, see page 129.)

**The Factor of Birth Trauma in Cancer of the Uterine Cervix.** Dr. Catharine Macfarlane. (For original article, see page 133.)

Discussion by Drs. J. A. McGlinn and P. F. Williams.

**The Treatment of Abruptio Placentae.** Dr. John A. McGlinn and Dr. W. B. Harer.

**Hormonic Induction of Menstruation in Amenorrheas of From Three Months' to Nine Years' Duration.** Dr. Charles W. Dunn.

Discussion by Drs. C. Mazer, J. Hoffman and F. L. Payne.

---

## BROOKLYN GYNECOLOGICAL SOCIETY

*MEETING OF MARCH 1, 1935*

The following paper and case reports were presented:

**Torsion of the Pregnant Uterus With Kyphotic Pelvis.** Dr. B. Rabbiner. (For original article see page 136.)

**Melanoma of the Urethra.** Dr. A. H. Rosenthal (by invitation.) (For original article see page 115.)

**Choice of Cesarean Section.** Dr. H. C. Williamson.

---

## CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF DECEMBER 21, 1934*

The following papers were presented:

**Hemorrhage in Late Pregnancy.** Dr. Philip H. Smith. (For original article see page 62.)

**Placenta Previa.** Dr. David S. Hillis.

**The Rôle of Transfusion in the Treatment of Obstetric Hemorrhage.** Dr. Wm. J. Dieckmann and Dr. Edwin F. Daily. (For original article see page 1.)

---

*MEETING OF JANUARY 18, 1935*

The following case reports were presented:

(1) **Sarcoma and Adenocarcinoma of Body of Uterus; Adenocarcinoma of Cervix.** (For original article see page 143.) (2) **Squamous Cell Carcinoma of Cervix; Adenocarcinoma of Fundus of Uterus.** (For original article, see page 137.) (3) **Nonpolypoid Sarcoma of Cervix Uteri.** (For original article, see page 145.) All by Dr. Mark T. Goldstine.



# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

## Selected Abstracts

### Uterine Carcinoma

Fahmy, E. Chalmers: An Analysis of 937 Cases of Post-Menopausal Hemorrhage, *J. Obst. & Gynec. Brit. Emp.* 40: 506, 1933.

Among the 937 cases of postmenopausal hemorrhage, a definite disease entity of anatomic origin was found in 796 women (85.0 per cent). Functional bleeding, therefore, constitutes a small group of only 15.0 per cent. Bleeding in 43.1 per cent of the total cases was of malignant origin. Of this group nearly three-fourths, or 35.5 per cent of the total series had uterine cancer. The author concludes, "that a fairly constant, moderate hemorrhage extending over many weeks is probably, though not necessarily, of malignant origin."

WILLIAM F. MENGERT.

Schultz, W.: Corpus Bleeding in Old Women, *Monatsschr. f. Geburtsh. u. Gynäk.* 95: 76, 1933.

Schultz emphasizes that not all bleeding which occurs in old women is due to carcinoma. He bases this statement upon a series of 232 cases of bleeding in elderly women observed in the Koenigsberg clinic. In the cases where bleeding came from the body of the uterus only one-tenth were due to malignancy. In more than half of the remainder of these cases the source of the bleeding was inflammatory necrotic processes in the endometrium. In some cases hyperplasia was found and in others polyps were present. Most of the latter were situated in the tubal corners. In some instances disturbances in the circulation such as hypertension were the cause of the bleeding. In six cases ovarian tumors were associated with the uterine bleeding but in only one of these six cases was the ovarian tumor responsible for the bleeding.

When bleeding from the body of the uterus occurs, we should first think of carcinoma but if this is ruled out by curettement, the latter treatment usually suffices to produce a cure.

J. P. GREENHILL.

Tourneux, J. P.: Cancer of the Cervix in Cases of Uterine Prolapse, *Gynécologie* 33: 273, 1934.

In the French literature there are reports of only five cases of prolapse of the uterus associated with cancer. Tourneux adds a sixth case. Among the 27 cases reported in the entire literature most women were between 60 and 70 years of age.

The treatment of choice is vaginal hysterectomy. The many theories advanced to explain the infrequency of the association of cancer of uterine prolapse are unsatisfactory.

J. P. GREENHILL.

Haegler, H.: The Coincidence of Uterine Prolapse and Carcinoma of the Portio, *Arch. f. Gynäk.* 150: 135, 1933.

Carcinoma rarely develops in the prolapsed uterus, there being less than twenty such cases reported in the literature. The author reports five instances occurring among 11,045 women seen in the second Frauenklinik in Vienna between 1926 and 1931. He also adds two others seen by Weibel in Prag. This gives an incidence of 1.2 per cent among the 395 women suffering from prolapse, while the incidence among the women without prolapse was 7.2 per cent. Such a decrease in the incidence of carcinoma of the cervix in the presence of prolapse of the uterus must be an argument against the theory that chronic irritation is a causative factor in the production of cervical carcinoma. No other type of cervix is exposed to the constant trauma, irritation, inflammation and infection as is the cervix of prolapsus. The author believes that this may be due to the drying out and cornification of the superficial epithelium which prevents not only growth but also development of carcinoma. It may be possible that the lack of secretion literally starves out malignant growths.

RALPH A. REIS.

Jorstad, Louis H., and Auer, Eugene S.: Histological Grading in Carcinoma of Uterine Cervix, *Surg. Gynec. Obst.* 57: 583, 1933.

Considerable interest has been aroused in regard to the significance of the grading of carcinoma since the publication of Broders' work in 1921. Broders has arbitrarily divided tumors into four grades.

Adverse criticism of grading is sometimes based on the fact that different grades are found in different portions of the same tumor and at different periods of growth there is a difference in the grade of the tumor. This may be due to the resistance of the host at varying periods of time. Additional adverse criticism is based on the personal equation.

Some clinicians have attempted to formulate conclusions in regard to the prognosis of cervical (uterine) cancer, based on the results of numerous studies on grading of carcinoma of the lower lip. It is impossible to use the lip as a basis of comparison for tumors of the cervix, simply on the assumption that in both instances we deal with surface epithelium.

From a comparison made of an unselected series of squamous cell carcinoma of the lower lip and squamous cell carcinoma of the cervix, it is clearly seen that the two are entirely dissimilar. In cancer of the lip we see 26 per cent of all cases in Grade I, whereas but 1.3 per cent of the cervical cancers are thus grouped.

Cancers of the cervix treated by radium alone have been arranged into clinical groups as well as microscopic grades, using the clinical grouping of the Schmitz classification, which divides cancer of the cervix into groups as follows: Group I, malignancy is confined to the uterine cervix; Group II, malignancy has spread to the adjacent vaginal wall; Group III, uterus is still movable, but there is beginning thickening of one or both broad ligaments; and Group IV, uterus is fixed.

From a study of this chart it seems evident that from a prognostic viewpoint clinical grouping and extent of disease is more important than grading. This signifies that grading alone is of no value although it is or may be of great value

in the radium treatment of a specific case of carcinoma of the cervix, in fact it may be the deciding factor in the decision to employ surgical treatment rather than radiation, or vice versa.

WILLIAM C. HENSKE.

**Chambers, H.:** Histological Classification of Cancers of Uterine Cervix and Relation of Growth Structure and the Results of Radium Treatment, *Am. J. Cancer* 23: 1, 1935.

The biopsy material from 728 cases of cancer of the cervix has been examined and 500 cases have been histologically graded, 228 being unsuitable for classification.

The results of treatment are recorded with special reference to local cure of the cancer at the primary site in relation to the histologic type. The highest percentage of local cures has been obtained in the transitional type of squamous cancer Grade III, 73.8 per cent, and in the adenocarcinomas, 72.9 per cent, but none of the histologic grades show a difference of more than 15 per cent in either local cure or in the number of three-year survivors. There is no evidence in this material that adenocarcinomas are insensitive to radiation.

HUGO EHRENFEST.

---

## Items

---

### New Officers of the American Gynecological Society Elected at the Hot Springs Meeting

*President*, Benjamin P. Watson, New York, N. Y.

*Vice-Presidents*, William A. Scott, Toronto, Canada, and John A. McGlenn, Philadelphia, Pa.

*Treasurer*, William C. Danforth, Evanston, Ill.

*Secretary*, Otto H. Schwarz, St. Louis, Mo.

---

### Awards for Scientific Exhibits at Annual Meeting of the American Medical Association, Atlantic City, N. J., June, 1935

The Gold Medal to F. L. ADAIR and M. EDWARD DAVIS, Department of Obstetrics and Gynecology, University of Chicago, for original investigations in the development of ergot as a therapeutic agent and especially of a new active principle isolated in crystalline state from ergot, together with its pharmacologic and medicinal properties. An article describing this research in full will be published in the October issue of the JOURNAL.

AARON E. KANTER, CARL P. BAUER and ARTHUR H. KRAWANS, Rush Medical College of the University of Chicago, for exhibit illustrating a new biologic test for hormones in pregnancy urine.

---

### Pacific Coast Society of Obstetrics and Gynecology

The Annual Meeting of the Pacific Coast Society of Obstetrics and Gynecology is to be held in Los Angeles, California, November 6 and 9, 1935.

## Correspondence

---

### The Value of the Bitterling Test for Pregnancy

IN A preliminary report rendered by Kanter, Bauer, and Klawans, substantial praise was given to a new test for pregnancy in which a fish, the Japanese bitterling, was utilized as the biologic test species. The test was presumably based on the reactivity of the ovipositor of this fish to an excess, probably, of the estrogenic hormone in the urine of pregnancy.\* Normally, this ovipositor is readily seen in the female bitterling as a projection about 2 mm. long just anterior to the ventral fin. During the breeding season and (according to the authors) in response to approximately 40 to 120 mouse units of estrin in pregnancy urine, this ovipositor enlarges to between 15 and 25 mm. in length, so that it is easily visible. The many advantages cited over the usual pregnancy tests, led us to investigate its potentialities.

At the outset of our experimentation we were impressed by the apparent impracticability of the "bitterling test," both because of the heavy mortality of the fish attendant upon their handling and because of the impossibility of standardizing the specimens as required in the original article. We were fortunate in securing a quantity of these fish through the cooperation of the Bureau of Fisheries in Washington, through whose efforts we were placed in contact with importers in San Francisco. In the first shipment a high mortality resulted notwithstanding consultation with the Bureau of Fisheries. About ten survived but these too, succumbed after some preliminary work in testing. To our surprise, when our second shipment arrived, twenty out of ninety-seven already showed a visible elongation of the ovipositor. This unaccountable feature subsided, however, after twenty-four hours in our tanks.

The standardization process referred to in the original article was attempted, but very early in our work the futility of it was recognized. The process required that we select only those fish which reacted positively to positive urine and negatively to negative urine. The test is presumably based on stimulating the ovipositor with estrogenic substance; the quantity which should yield a positive test is, according to the authors, 40 to 120 mouse units. It is our contention that this estimate is much too high, that much smaller quantities of estrin will yield a positive test. Not only may there be an individual sensitivity in the fish, but even this is variable according to factors as yet undiscovered by the authors of the original article or by ourselves. In fact, 4 c.c. of urine, which is the quantity used in the test, will yield only 20 mouse units at the beginning of pregnancy and about 40 mouse units at its termination.

When we checked the urine of regularly menstruating, nonpregnant women, in whom 4 c.c. would yield only 0.4 to 0.8 of a mouse unit of estrin, our results were quite unexpected. In nine definitely negative cases as checked clinically and by the Aschheim-Zondek reaction, seven were strongly positive according to the "bitterling test," one moderately positive and only one negative. The negative

---

\*Kanter, A. E., Bauer, C. P., and Klawans, A. H.: A New Biologic Test for Hormones in Pregnancy Urine, *J. A. M. A.* 103: 2026, 1934.

test was obtained in a fish that died within the first twenty-four hours of the test, and it is quite possible that this occurred before it had a chance to react.

In normal, healthy human males, the urinary output of the male sex hormone in 4 c.c. of urine would be only 2 mouse units. Yet witness the effrontery of this foreign visitor in slandering ten of our male citizenry by declaring six of them strongly positive and two moderately so. The other two fish died. The male hormone, it might be added, while chemically related, is biologically identical with the female sex hormone.

Twelve cases of well-advanced pregnancy were then submitted to the "bitterling test." The A-Z test in all these cases was, as usual, definitely positive. In the "bitterling test," six were strongly positive, four only moderately so, one was negative and one died a negative.

Three cases of hydatid mole were tested on five fish, of which two died at once. One gave a negative reaction, although here again, the A-Z test was positive, and two of the fish gave strongly positive results.

Thus we see positive reactions in the presence of very minute quantities of estrin and in one instance, where transportation alone excited growth of the ovipositor. There is no apparent gradation in reaction as witness the great number of positive tests in the nonpregnant and in the male as well as the variability of reaction in definitely positive urines. Since the quantity necessary for a positive reaction is so infinitely small, the value of this test begins to shrink to negligible proportions. One of us (Kotz) has recently shown there is a marked increase of estrin in the urine in cases of functional dysmenorrhea. Here again, a positive pregnancy test would only confuse the diagnosis.

Thus in summary we may state that thirty-six tests were performed on these Japanese bitterlings in an attempt to standardize this fish for use in biologic pregnancy tests. Twelve known positive urines yielded six strongly positive, four moderately positive, one questionable negative reaction. Nine definitely negative cases yielded seven strongly positive results and only one negative. Ten male urines yielded eight strongly positive, one questionable positive test for pregnancy. The results in hydatidiform mole were conflicting. Therefore we believe this test to be of no practical value in the determination of pregnancy. It is based on an incorrect premise that the fish will yield positive results only in the presence of 40 to 120 mouse units of estrin. Were these figures correct, the test as published would be positive only in the later periods of gestation. As a matter of fact, these fish react to much smaller quantities. Standardization of the fish has been a hopeless gesture in our hands, although we followed the published technic and used the exact species of fish as advocated in the original article.

A test using a tropical fish is impractical, even if the test itself is of value. The fish are not easy to handle and have a heavy mortality rate, making them more expensive in the long run than mice.

A biologic pregnancy test based on small amounts of increase in urinary estrin is of no value as the possibilities of error in allied causes with some estrin increase, such as dysmenorrhea, are great and limit its usefulness.

In our own experience we have found the Aschheim-Zondek and the Friedman tests useful and dependable diagnostic aids and not prohibitive from an economic point of view.

J. KOTZ, F.A.C.S., M.D.

H. S. DOUGLAS, A.B., M.D.

E. PARKER, A.B., M.A., M.D.

GEORGE WASHINGTON UNIVERSITY MEDICAL SCHOOL.  
DIVISION OF ENDOCRINOLOGY  
WASHINGTON, D. C.

## Technic Fothergill Operation

To the Editor:

IN THE February issue of this JOURNAL (page 240) Dr. Robert T. Frank describes in considerable detail and with excellent illustrations, the technic of the Fothergill operation. I, too, have had considerable experience with this procedure and wish to call attention to a minor, but to my mind very important, difference in the method of placing the sutures to draw the flaps into the cervical canal.

In Fig. 1 A (one half of Dr. Frank's Fig. 4) suture number 1 is shown passing *under* the edge of the flap of vaginal mucosa, the "bite" being on the surface. In Fig. 1 B is shown the method I use. The suture is brought *over* the edge of the flap and the "bite" is underneath. In Fig. 2 A is shown in longitudinal section what happens with Dr. Frank's technic, and in Fig. 2 B with mine, when the suture is tightened and the flaps are drawn into the cervical canal. With his technic the edges of the flaps are everted and puckered up. This is counterbalanced to some extent by the insertion of the packing which pushes down and holds the

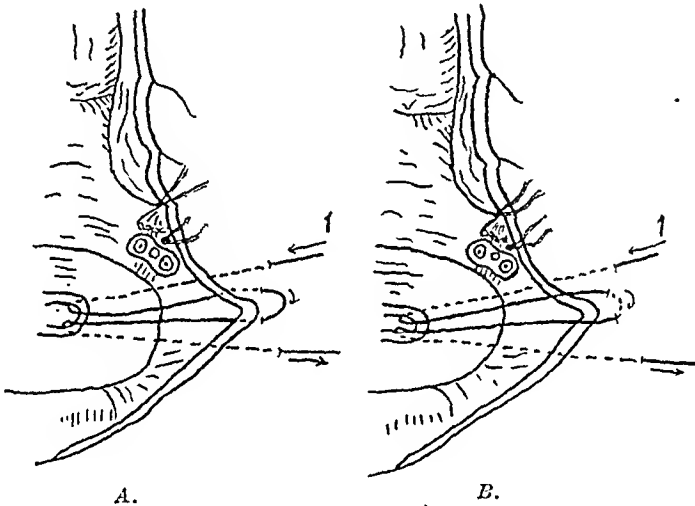


Fig. 1.—A shows Dr. Frank's method of passing sutures under the edge of the mucosal flap. B shows the suture passed over the edge of the flap.

edges flat against the walls of the cervical canal. As this canal is lined by mucosa which has been everted away, perhaps completely, perhaps not, there is no certainty that the raw undersurfaces will adhere firmly in the four days that the packing is allowed to remain. If they should not adhere firmly, they will, on withdrawing the packing, evert again. This is avoided entirely by my method because the sutures by passing over the edges hold them down in close apposition to the canal walls for the life of the suture (ordinarily 10-day catgut). This same principle applies to all four sutures.

I can corroborate all that Dr. Frank has said about the results of the operation except in third-degree prolapse. A careful study of the follow-up results in a series of nine hundred cases of vaginal plastics has convinced me that it is impossible to evaluate results under twenty-four months of observation. A large part of Dr. Frank's sixty-seven cases is less than two years old and there are only eleven cases of third degree prolapse all told among them. Dr. Frank has probably only half a dozen or so third-degree prolapse cases (a rather small number) which have been observed long enough for critical purposes. I fear that he may have jumped at conclusions which he will be compelled to revise later. I, too, was en-

thusiastic at first but further observation of some of these same cases has raised an element of doubt in my mind, and I prefer to reserve judgment until a larger number of cases has been observed sufficiently to warrant the expression of an opinion.

This operation in suitable cases has certain additional advantages which Dr. Frank did not sufficiently emphasize. They are (1) it is very easy to teach to

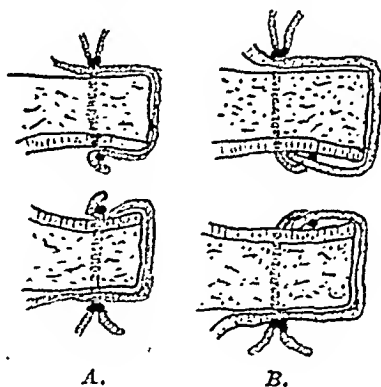


Fig. 2.—A, when the suture is tightened the edges of the flap are everted and puckered in Dr. Frank's method. B, in this method the suture holds the edges of the flap smoothly against the walls of the cervical canal.

junior staff men. (2) It can be done rapidly; thirty minutes is ample time. (3) One procedure takes care of cystocele, cervix and prolapse and any type of perineorrhaphy can be combined with it. (4) Even a poor operator can learn it and get better results with it than with most other operations for prolapse.

HOWARD E. LINDEMAN, M.D.

135 CENTRAL PARK, WEST  
NEW YORK CITY.

---

Guthmann, H., and Stahler, F.: The Influence of the Position and Function of the Intestinal Canal During Normal Pregnancy, *Monatsch. Geburtsh. u. Gynäk.* 93: 327, 1933.

The authors examined 23 healthy gravid women between the seventh and tenth month to determine the changes which occurred in the position and function of the intestinal canal. They found that there was a diminution in the tonus of the entire gastrointestinal tract. The gravid uterus acts on all parts of this tract as a dislocating organ. The parts mostly involved are the stomach, the last loops of the ileum, the lower sigmoid, and the rectum. The cardiac end of the stomach became relaxed and was less able to contract and this explains the frequent occurrence of heartburn in pregnancy. In one case of severe vomiting of pregnancy, there was a cardiospasm in the presence of hypotonicity of the esophagus. In the second half of gestation, the lower pole of the cecum is a handbreadth higher and about 2 fingers more laterally than in the nonpregnant state. Therefore, the appendix is dislocated accordingly. The time required for the passage of the intestinal contents is normal up to the sigmoid but in this organ there is a block. Hence constipation in pregnancy is mostly rectal in origin.

J. P. GREENHILL.

# American Journal of Obstetrics and Gynecology

---

VOL. 30

ST. LOUIS, AUGUST, 1935

NO. 2

---

## Original Communications

---

### A PARALLEL STUDY OF LABOR IN YOUNG AND OLD PRIMIPARAS\*

BASED UPON A CRITICAL ANALYSIS OF 372 CASES BELOW TWENTY  
AND ABOVE THIRTY-FIVE YEARS OF AGE

JOSEPH N. NATHANSON, M.D., NEW YORK, N. Y.

*(From the Woman's Hospital)*

WITHIN the past two decades, late marriage and low birth rate have become important aspects of a world-wide economic and sociologic upheaval. Many women are purposely avoiding maternity on the ground that they are too old to bear children without great hazard to themselves. In addition, such women are very often unfavorably influenced by the belief of the laity in a frequently dangerous, and occasionally even fatal issue in such a labor. This erroneous supposition is immediately given additional weight by haphazard lay and at times, quasi-scientific medical advice. It seemed, therefore, that it would be profitable to undertake a critical analysis of labor on a comparative basis, in young and old primiparas, in an effort to arrive at reasonably accurate conclusions.

The question at once arises, however, who is an old primipara? A careful survey of the leading textbooks on obstetrics and the literature in general fails to disclose a unanimity of opinion on this important phase of the subject, age limits from twenty-eight years to forty years having been employed by various authors. I have therefore chosen elderly white primiparas of thirty-five years and over, from the ward

---

\*Read by invitation before The New York Obstetrical Society, January 9, 1934.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



and private services of the Woman's Hospital, New York, and compared them to a similar group of women twenty years and under, as the primary objective was to study diametrically opposed groups of patients who were being subjected for the first time to the tests of labor at or near full term.

#### AGE DISTRIBUTION OF CASES

In Chart 1 the age distribution of the cases is shown both graphically and numerically. It will be noted that in the series of young primiparas, the largest number occurred in the twenty year group, whereas the

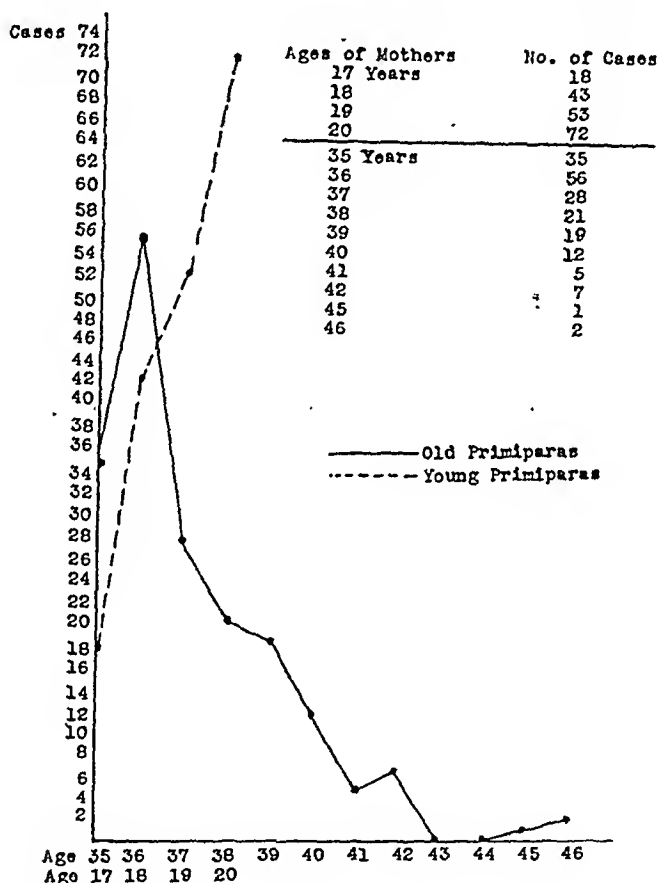


Chart 1.—Age distribution of cases in young and old primiparas.

majority of cases of the old primiparas were present in the thirty-six-year group, although the extreme age limits for both groups were seventeen years and forty-six years, two cases of the latter being found among the old patients.

#### TYPES OF PELVES

Chart 2 shows the types of pelves encountered in both young and old groups. It is rather significant to note that a higher percentage of normal pelves occurred in the old primiparas than in the young patients. Of the abnormal types of pelves, however, the just minor class occurred in 17.32 per cent of the cases in the young primiparas, and in only 7.69

per cent of the old patients. There was only a slight difference in the incidence of the simple flat pelvis in both groups, but the funnel or male type of pelvis occurred one and one-half times as often in the old primiparas as compared to the younger group. Stated in other terms, from the practical standpoint, if dystocia of bony origin is to be encountered, it would appear that the difficulty would be more frequent at the inlet in the young primipara, and at the outlet in her older sister.

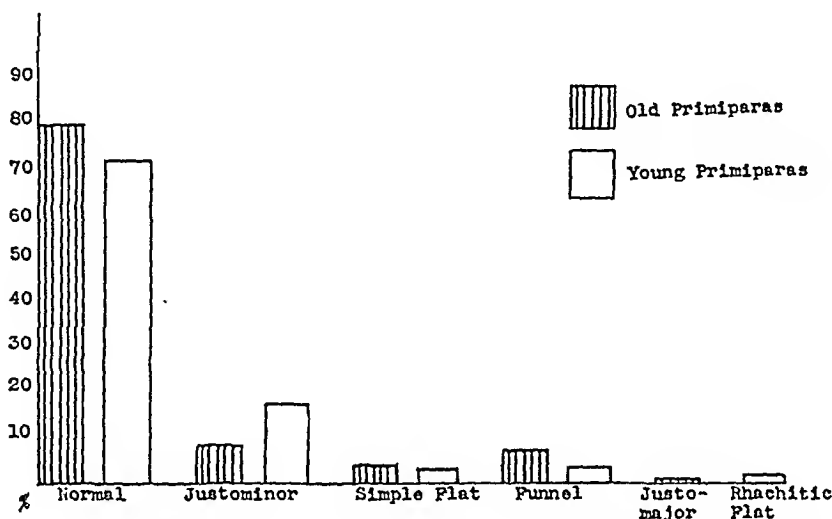


Chart 2.—Types of pelvis encountered in young and old primiparas.

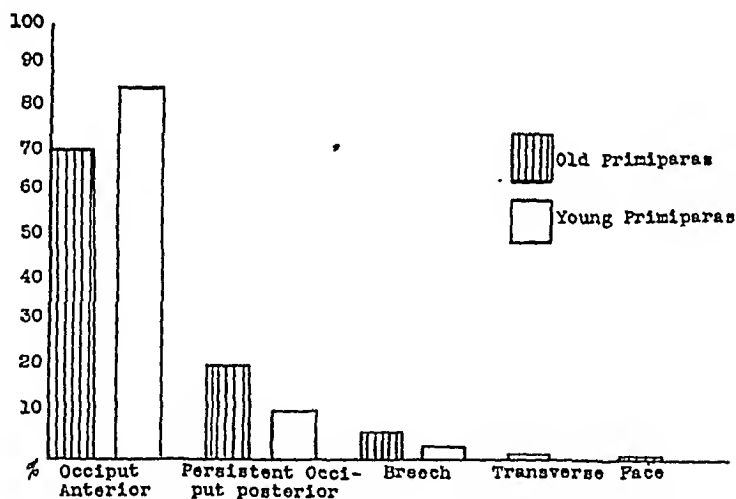


Chart 3.—Presentations and positions encountered in young and old primiparas.

#### PRESENTATIONS AND POSITIONS

Chart 3 sheds some rather interesting data. While the occipito-anterior position occurred in 85.71 per cent of the young primiparas, its incidence in the old group was 71.33 per cent. Occipitoposterior positions of the persistent type, however, were twice as frequent in the old primiparas as in the young ones, the readings being 21.94 per cent and 10.28 per cent, respectively. Breech presentations were also approximately twice as frequently encountered (6.09 per cent) in the old patients

as in the young primiparas (3.42 per cent). Practically the same ratio has been reported by Schulze and Nixon in their series of old primiparas. The very low incidence of the less frequent malpresentations (face, transverse, etc.) does not permit any deductions to be drawn. The interpretation of the figures presented in this table undoubtedly warrants the conclusion that persistent occipitoposterior positions and breech presentations occur twice as often in the old primiparas as in the younger patients, and undoubtedly constitute important contributing factors responsible for the longer labors and more particularly for the greater incidence of operative interference in old primiparas.

#### RUPTURE OF THE MEMBRANES

The time of the rupture of the membranes in relation to the various stages of labor, and its effect upon the duration of labor still remains a

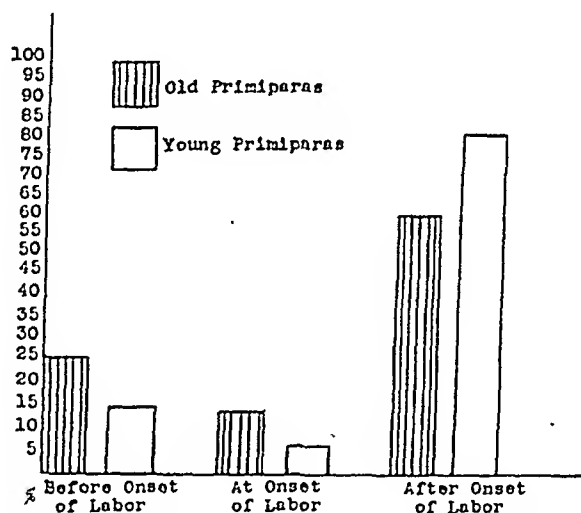


Chart 4.—Occurrence of rupture of membranes (spontaneous) in young and old primiparas in relation to onset of labor.

moot question among obstetricians. In view of the fact therefore, that there was only a difference of 11 per cent as affecting the old primiparas in the incidence of premature rupture of the membranes, I feel that no definite conclusions are warranted. It is interesting to record that similar findings were obtained by Essen-Möller and Linden who coincide with the opinion expressed in this communication on the rupture of the membranes in relation to labor, in old primiparas.

#### DURATION OF PREGNANCY

From time to time assertions have been made that pregnancy is of longer duration in the old primipara than in her younger sister. One, of course, is quite willing and, in fact, forced to admit that the actual duration of pregnancy is extremely difficult, if at all possible to estimate. Nevertheless, employing the usually adopted rule, it is surprising to

note that the average duration of pregnancy in the young group of patients was 281.33 days as contrasted to 279.42 days in the old primiparas. In other words, pregnancy was actually of longer duration in the group of younger patients in this series, as shown in Chart 5.

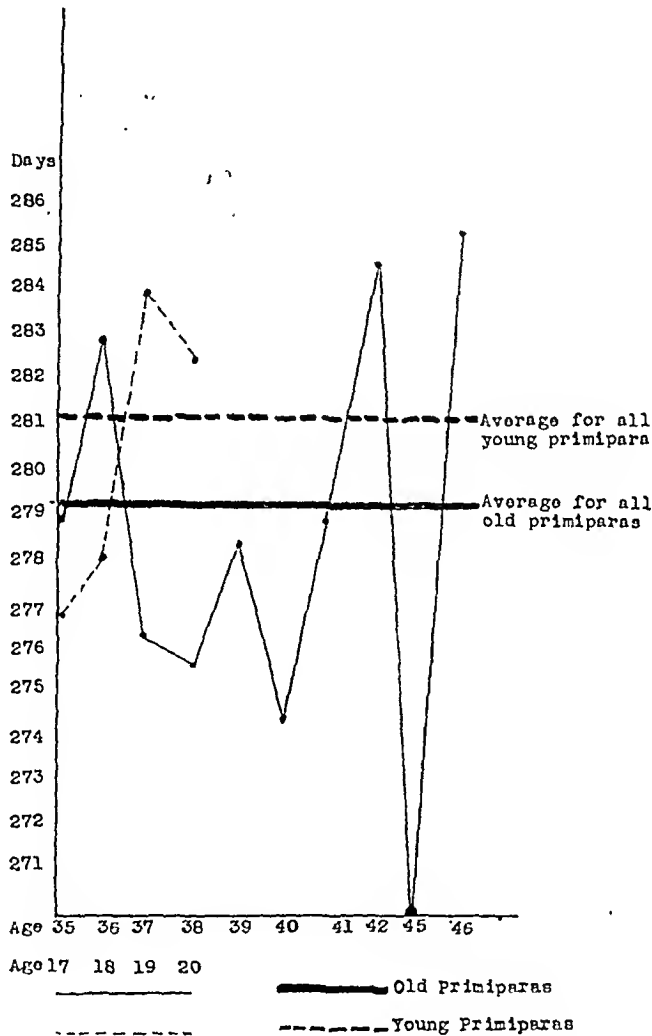


Chart 5.—Average duration of pregnancy (in days) in various age groups of young and old primiparas.

#### DURATION OF LABOR

It has been repeatedly stated by most writers and indeed it is the common belief of most obstetricians that the duration of labor among old primiparas is usually longer than in the young patients. This is definitely substantiated by the findings in this series as shown in Chart 6, and is a confirmation of the reports of other writers, notably Harris, Schulze, Nixon, and Daichman, but at variance with that of Quigley. The difference is most marked in the first stage where the average duration was seventeen hours and twelve minutes, and twelve hours and forty-eight minutes for the old and young primiparas, respectively. The average duration of the second stage was one hour and thirty-four

minutes in the old patients as compared to one hour and nineteen minutes for the patients in the young group. Oddly enough the duration of the third stage was slightly longer in the young group in whom the time was twenty-three and one-half minutes as compared to seventeen minutes for the old patients, in whom as it will be seen later, complications of the third stage were more frequently encountered.

In view of the fact that there is only a slight difference in the weight of the children in either group as is shown in Chart 9, the relatively short labor in the patients cannot be adequately explained on the ground that the baby is small, but rather that it is dependent upon a combination of factors, notably the greater incidence of abnormal presentations among the old patients, and especially the greater elasticity of the soft parts of the young primiparas.

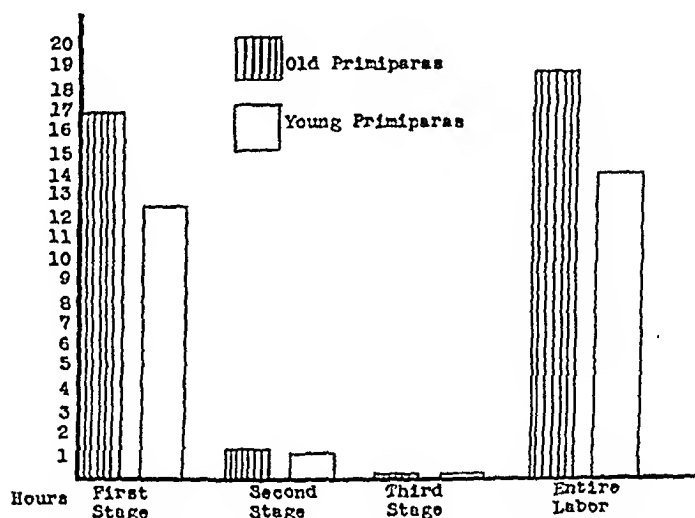


Chart 6.—Average duration of labor in young and old primiparas.

#### TERMINATION OF LABOR

Chart 7 is productive of some rather interesting findings. At the outset however, it must be stated that prophylactic low forceps and episiotomy is a very common elective procedure in many primiparas on the ward service and certainly is very frequently practiced by the members of the courtesy staff of the hospital. Hence, the cases terminated by low forceps do not actually enter into the final conclusions. The complete figures are as follows: Labor terminated spontaneously in 11.83 per cent of the old patients as compared to 31.21 per cent of the younger group, while prophylactic low forceps was employed in 46.77 per cent of the older patients and in 53.76 per cent of the young primiparas. When, however, one investigates the incidence of major obstetric procedures, interesting data are at once evident. Midforceps operations were employed in 20.45 per cent of cases of the older patients as contrasted to 10.21 per cent in the younger group. One high forceps was done in

one case of each group. Breech extraction was performed in 4.83 per cent of the old primiparas, and in 2.68 per cent of the younger patients, while internal podalic version was done in 4.3 per cent of cases of the old patients, and in only 1.61 per cent of the younger group. It is to be noted that craniotomy was not resorted to in either class of patients. The necessity for the greater frequency of major obstetric procedures excluding cesarean section in the older patients is, I feel, very closely allied to the greater incidence of inertia uteri, persistent occipitoposterior positions, and breech presentations in this group as shown in Chart 3.

We now come to the question of cesarean section, and here there is undoubtedly such a marked discrepancy in its incidence in both groups as to call for very close study of this phase of the subject. The opera-

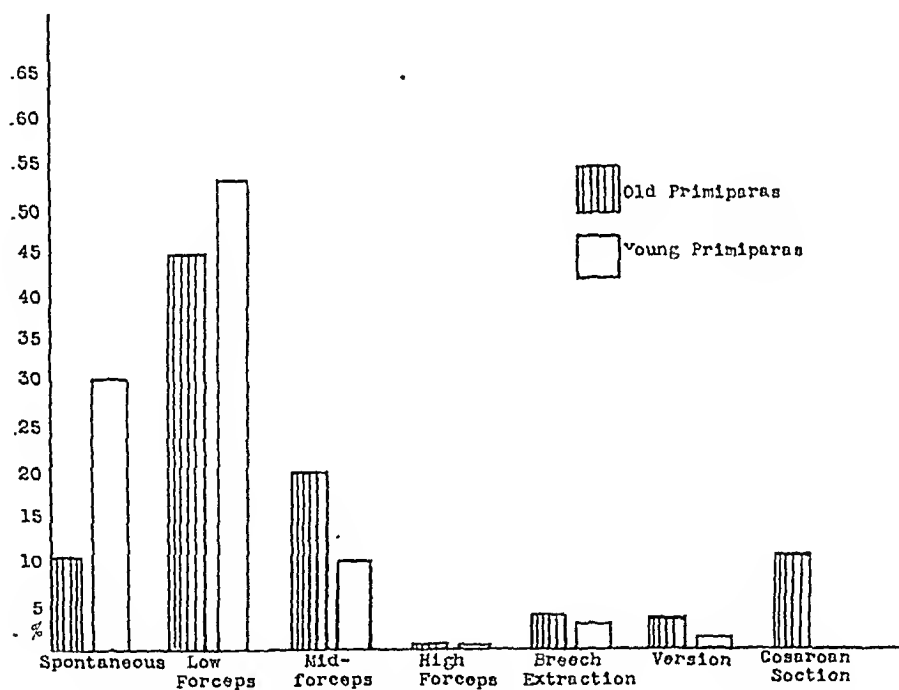


Chart 7.—Termination of labor in young and old primiparas.

tion was performed in twenty cases, or 10.75 per cent of the old primiparas, while no patient in the younger group was subjected to cesarean section. Quigley reported an incidence of 11.4 per cent in his series of old primiparas of thirty years and over, while in Daichman's series of patients over forty years of age cesarean section was performed in 23 per cent of the cases. The indications which account for the high incidence of the operation in the older group are shown in the brief synopses of the individual cases in Table I.

An impartial analysis of these cases must, I feel, lead to the conclusion that in practically every instance cesarean section was definitely indicated on more than one premise, the most important of which was *not* the advanced age of the patient. The definite existence of various degrees of pelvic deformity usually associated with other potent contribut-

TABLE I. INDICATIONS FOR CESAREAN SECTION IN OLD PRIMIPARAS

AGE	INDICATIONS	OPERATION	MOTHER	BABY
35	True cervical dystocia after trial labor of 18 hours	Low-flap	Living	Living
35	Marked funnel pelvis	Low-flap	Living	Living
35	Justominor pelvis with large baby at term. Mother had moderate bleeding during eighth month of pregnancy. Baby weighed 9 pounds 11 ounces	Classical (elective)	Living	Living
36	Membranes ruptured ten hours before onset of labor, cervix rigid and nonyielding, no advance after several hours of good uterine contractions; mother exhibited slight cardiac arrhythmia	Low-flap under spinal anesthesia	Living	Living
36	Justominor pelvis, unengaged head, secondary inertia uteri, irregular labor of 18 hours	Low-flap	Living	Living
36	Marked hepatic toxemia in last month, with marked jaundice and marked liver disturbance substantiated by chemical studies and liver function tests. No improvement in spite of vigorous antitoxic treatment	Low-flap	Living	Living
37	Justominor pelvis with true conjugate of only 8 cm.; breech presentation	Classical (elective)	Living	Living
37	Uterus contained a large fibroid which produced bleeding during the first five or six missed periods. In addition patient had moderate toxemia	Elective low-flap followed by supraeervical hysterectomy	Living	Living
37	Failure of head to engage in presence of male pelvis and overriding of symphysis after trial labor of 50 hours	Low-flap	Living	Living
37	Simple flat pelvis, persistent mento-posterior position, rigid cervix which did not yield after trial labor and rupture of membranes seven hours prior to onset of labor	Low-flap	Living	Living
38	Marked funnel pelvis with deep symphysis. Patient weighed 210 pounds at term	Low-flap (elective)	Living	Living
38	Marked rectal stricture following previous Whitehead operation	Classical (elective)	Living	Living
39	Multiple fibromyomas of uterus, premature rupture of membranes at term; patient weighed 225 pounds	Low-flap	Living	Living
40	Patient weighed 266 pounds and was treated for hypertension and toxemia for several weeks; urine showed granular and hyaline casts; uterus contained multiple fibroids	Elective classical under spinal anesthesia, followed by hysterectomy	Living	Living
41	Marked funnel pelvis, large baby	Classical (elective)	Living	Living

TABLE I—CONT'D

AGE	INDICATIONS	OPERATION	MOTHER	BABY
41	Marked toxemia, with no improvement under conservative treatment. Patient had a threatened miscarriage in tenth week. Uterus contained a few small fibroids	Low-flap	P.P. phlebitis recovered	Dead; had many anomalies
42	Premature rupture of membranes, trial labor of 16 hours, nonengagement of head, nonyielding cervix, in presence of just minor pelvis of moderate degree, and persistent occipitoposterior position	Low-flap	Living	Living
45	Married twenty-seven years, no previous pregnancies, funnel pelvis, unengaged head. Patient died on seventh day postoperative of acute suppression of urine beginning twenty-four hours after operation. Terminal bronchopneumonia	Classical (elective) at term	Dead	Living
46	Married twenty years, no previous pregnancies; patient had asymptomatic lues with four-plus Kahn and Wassermann reaction. Treated by me during pregnancy. Baby weighed 8 pounds 10 ounces	Low-flap (elective)	Living	Living
46	Minor degree of pelvic contraction advanced age of patient. Patient had postpartum hemorrhage, transfusion, died within two hours after operation	Elective low-flap	Dead	Living (8 pounds 5 ounces)

ing factors such as a nonyielding cervix, pelvic neoplasms, progressive toxemia, etc., is noted in practically every case in this group.

While an incidence of 10 per cent of cesarean section may at first appear to be high and almost suggestive of radical obstetrics, nevertheless it is of utmost importance not to lose sight of the fact that in the case of the old primiparas so much is at stake that everything ought to be done to help her obtain a living child. In this connection therefore, it is interesting to compare the results obtained by the so-called conservative clinics. Nixon of London has recently reported a series of elderly primiparas in whom no cesarean sections were performed with a maternal mortality of 4 per cent, and a fetal mortality of 17 per cent; in other words, a maternal and fetal mortality three times and five times as high, respectively, as that reported in this study, notwithstanding our cesarean incidence of 10 per cent. Nixon, however, is frank to admit that the operation should have been resorted to in his series of cases.

Essen-Möller has reported a cesarean incidence of 7.76 per cent with a maternal mortality of 0.97 per cent for his entire series of old primiparas, and a fetal mortality of 8.25 per cent. Linden of Stockholm, who also follows ultraconservative procedures reports a series of cases in



elderly primiparas, in whom craniotomy was performed in 4 per cent of the cases with a total fetal mortality for the entire series of 8.8 per cent but no maternal deaths.

Notwithstanding however, the justifiability for the high incidence of cesarean section in this series, I am firmly convinced that if we were to subscribe inflexibly and to teach that the operation is indicated in every case of the old primipara, a gross exaggeration not based upon our present experience would be the result, for as will be seen from the cases contained in this communication, 89.25 per cent were delivered per vaginam. Even more significant is the fact that a considerable number of these patients were over forty years of age when they were delivered uneventfully of living children after comparatively short labors. In Quigley's series, 88.6 per cent of the old primiparas were also delivered per vias naturales.

#### INERTIA UTERI

It has been claimed by some writers that the part played by the rigidity of the soft tissues in elderly primiparas from the standpoint of prolonging the labor and producing dystocia, is problematical so far as it must be estimated objectively. It is important, therefore, to recall the investigations of Ogata, who found the uterus to be well supplied with connective tissue and poorly supplied with muscle tissue at the beginning and end of the period of sex maturity. He also showed that beginning with the twenty-sixth year there is a distinct deterioration which increases successively, as a result of which weak labor or inertia and rigidity of the soft tissues in the parturient canal of the elderly primipara obtain.

From the clinical study herewith presented one is firmly convinced that uterine inertia is a definite complication of labor in the old primipara. In this series, primary uterine inertia occurred in six cases of the old group, and was entirely absent in the young patients, while secondary inertia was present in three cases of the old primiparas and only once in the young group. The incidence of both primary and secondary inertia in the young and old patients, therefore, was 4.83 per cent and 0.53 per cent, respectively, a disparity sufficiently marked to stamp it as a potential factor to be contended with when delivering an old primipara.

#### INCIDENCE OF PELVIC NEOPLASMS

As would be expected there is a marked discrepancy in the incidence of pelvic neoplasms in both groups of patients. Fibromyomas of the uterus were present in fourteen cases or 7.52 per cent of the old primiparas as compared to two cases or 1.07 per cent of the young group. Ovarian cysts were encountered in only one case of the old patients, and an incidence of 0.53 per cent, and were absent in the entire group of young patients.

While the presence of these pelvic tumors cannot per se account for the greater incidence of operative deliveries in old primiparas, they nevertheless do constitute contributing factors to the more frequent necessity for the artificial aid rendered to this group of patients, and to the greater frequency of immediate postpartum complications, of which hemorrhage is an important one.

#### INCIDENCE OF STILLBIRTHS

The stillbirth mortality, excluding those cases where the fetal heart was not heard at the time of the admission of the patient to the hospital, was 3.20 per cent and 1.06 per cent in the old and young groups, respectively. The various causes of these fetal deaths are herewith appended, but the fact that the incidence was three times as high in the children born to the older patients entitles it to an important place in the conclusions of such a study, notwithstanding whatever causes we may assign to it as an explanation. Essen-Möller reported a fetal mortality of 8.25 per cent, Linden 8.8 per cent, Nixon 17 per cent, and Quigley 5 per cent stillbirth incidence in their series of old primiparas.

#### MATERNAL MORTALITY

Here again the old primiparas showed a greater tendency to an unfavorable outcome than did their younger sisters. There was no maternal death among the young patients, while three deaths occurred among the older group, a maternal mortality of 1.61 per cent. A synopsis of these cases shows that hemorrhage was responsible for two deaths, while failing kidney function, most probably with an old standing but undetected renal pathology, accounted for the third death on the seventh day following elective cesarean section, in a primipara forty-five years of age.

#### SEX OF CHILDREN

It has been stated by various authors that elderly primiparas give birth to more male children than do younger women. In this series, 51.87 per cent of the children born to the older patients were males as compared to 47.87 per cent of male children born to the younger group. This is practically the same percentage as is found for all children delivered by all types of patients, the usually accepted ratio being 51.20 per cent and 48.80 per cent for male and female children, respectively.

#### WEIGHT AND LENGTH OF CHILDREN

Assertions have been made by a number of writers that old primiparas tend to give birth to larger children than do young patients. On that account therefore, a careful study was made in this series to affirm or

deny the accuracy of such statements. The average weight as shown in Chart 9 for all children born to the old primiparas was seven pounds four and three-fourths ounces, as compared to seven pounds three and one-half ounces for the young group, with a tendency for the male children to be somewhat heavier than the female children. The average length for all children delivered by the old patients was 50 cm. as compared to 50.11 cm. for the children born to the young primiparas. Here again there was a very slight difference in favor of the male children in both groups.

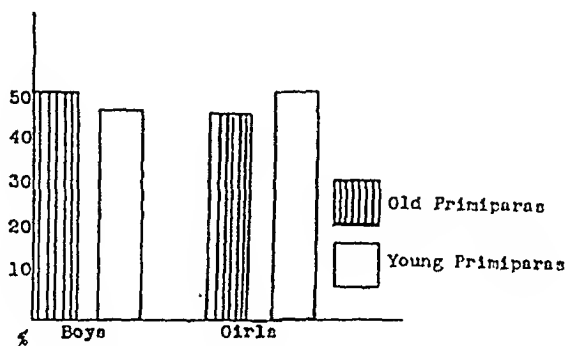


Chart 8.—Sex of children born to young and old primiparas.

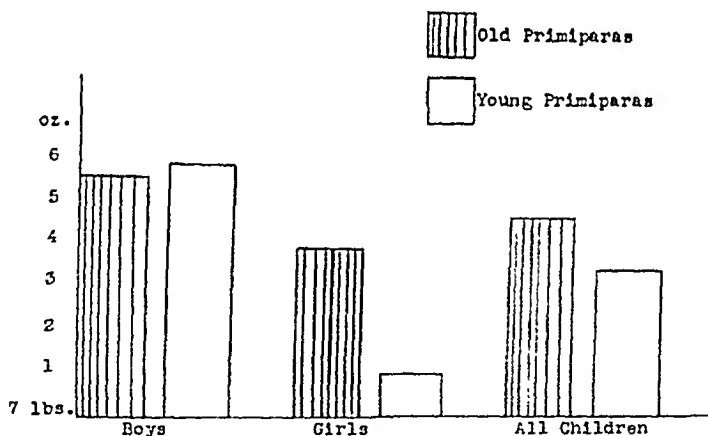


Chart 9.—Average weight of children born to young and old primiparas.

#### COMPLICATIONS DURING PREGNANCY AND LABOR

Mild toxemia occurred in thirteen cases or in 6.98 per cent of the young patients and in seventeen cases of 9.13 per cent of the old group, while severe toxemia was encountered in four cases or 2.14 per cent of the old primiparas as compared to one case or 0.53 per cent of the young patients. In the antepartum period, pyelitis was present in one case or 0.53 per cent in each group, and in the postpartum period in three cases or 1.61 per cent of the old patients, and not at all in the young group. Sappremia was present in six cases or 3.20 per cent of the old primiparas, as compared to eleven cases or 6 per cent of the young patients. The

marked difference in these figures is difficult of explanation in the light of the greater frequency of major obstetric procedures among the older patients. It is also interesting to note the complete absence of placenta previa and premature separation of the placenta in both groups, thus confirming the generally accepted view that these lesions are more frequently encountered in multiparas than in primiparas.

Mastitis, either simple or suppurative, was not at all encountered among the old primiparas, but was present in eight cases or 4.30 per cent of the young patients. The only possible logical explanation for this finding is the fact that breast feeding was more frequently resorted to among the young patients, thus predisposing them to inflammatory processes affecting the breasts.

Of the immediate postpartum complications, hemorrhage was present in seven cases or 3.76 per cent of the old patients as compared to four cases or 2.14 per cent of the young group, while retained placenta occurred in two cases or 1.07 per cent of the old primiparas and not at all among the young patients. From this study therefore, we are justified in concluding that complications of the third stage of labor are twice as frequent in old as in young primiparas, and that toxemia occurs one and one-half times as often in the old patient as in her younger sister.

#### RELATION OF LABOR TO THE MENSTRUAL CYCLE

Considerable thought was given to the possible relation of the menstrual cycle of the patient to the type and particularly to the duration of labor in each case. While definite conclusions are not warranted, nevertheless some highly suggestive findings were present in a number of cases, and it is hoped that more extended studies will be possible at some future date in order to clarify this aspect of the subject. It is interesting to note, however, that where there was a definite history of irregularity in the menstrual function and particularly where menstruation was established rather later than usual, especially after the sixteenth year, labor in a number of cases was of longer duration than otherwise. As previously stated, however, one is not prepared to draw definite conclusions at the present time as the number of cases is too small to warrant indisputable positive deductions.

#### DURATION OF MARRIAGE PRIOR TO LABOR

There is a general opinion among obstetricians, which was first proposed by Leopold Meyer, that elderly primiparas who conceive for the first time after a number of years of marriage are prone to longer and more difficult labors than those who, although they may be advanced in years, become pregnant within a relatively short time after marriage. In eighty-two cases of old primiparas in this series, the exact length of time of marriage was known, and the average for this group was five years

and two months, with several patients who had been married more than twenty years. In thirteen patients who were married ten years or more prior to conception, labor lasted on an average eighteen hours and nineteen minutes which was less than the average duration for the entire series of old primiparas. In contrast to this, in thirty-two cases of old primiparas who had been married three years or less, the average duration of labor was eighteen hours and twenty-eight minutes. The findings in this study are thus at variance with the oft-repeated assumption that the time of marriage influences the duration of labor, and I am, therefore, unwilling to accept the validity of Meyer's postulates, upon which too much stress has been placed in the past, and one is led to the conclusion that too little importance is attached to the more important factors of varying degrees of pelvic contraction, inertia uteri, nonyielding cervix, abnormal presentations, etc.

#### SUMMARY AND CONCLUSIONS

1. It is suggested that for the sake of uniformity in future studies, that thirty-five years be chosen as the lower age limit for elderly primiparas.

2. The funnel pelvis was more frequently encountered among elderly primiparas and the justminor pelvis among their younger sisters in this series. Dystocia of bony origin, therefore, may be the more frequent complication at the inlet in the young patient, and at the outlet in the old primipara.

3. Persistent occipitoposterior positions and breech presentations occurred in 21.94 per cent and 6.09 per cent of cases, respectively in old primiparas, in whom the incidence of these abnormal findings was twice as high as in the young patients.

4. There was a difference of only 11 per cent in the incidence of premature rupture of the membranes in elderly primiparas as compared to that of young patients.

5. Labor was of definitely longer duration in the old primiparas, the greatest difference occurring in the first stage, and this is undoubtedly accounted for by the greater incidence of abnormal presentations and inertia uteri in the old patients, and by the greater elasticity of the soft tissues in the young primiparas.

6. Cesarean section was performed in 10.75 per cent of cases among the older patients and not at all in the young group. It is of utmost importance, however, to note that the age of the patient was *not* the major indication for the operation in most cases, such potent contributing factors as pelvic deformity, nonyielding cervix, progressive toxemia, etc., being present in the great majority of cases of the elderly primiparas in whom cesarean section was performed.

7. Inertia uteri, both primary and secondary, was nine times as frequent in the old as in the young patients, and is a potential factor to be contended with when delivering an old primipara.

8. The stillbirth incidence was three times as high among the children born to the older patients as compared with those of the mothers in the young group.

9. The maternal mortality in the elderly primiparas was 1.61 per cent, while none of the young mothers died as a result of pregnancy or labor.

10. The age of the primipara has little or no influence upon the sex, weight, or length of her children.

11. Toxemia occurred one and one-half times as often in the old patient as in her younger sister, while complications of the third stage of labor were twice as frequent in the former as in the latter.

12. Irregularities in menstruation, and particularly the late establishment of the function seemed to influence the type and duration of the labor.

13. From the findings in this series, the time of marriage does not appear to influence the duration of labor.

14. In the last analysis, on the basis of this study, no inflexible rules can be laid down for the routine conduct of labor in the elderly primipara. Individualization of each case with its concomitant demands, guided by the experience, judgment, and ability of the attending obstetrician, would appear to be the only ideal approach to the solution of the problem.

I desire to express my deep appreciation to Dr. George Gray Ward, Chief Surgeon of the Woman's Hospital, New York, for the privilege of allowing me to undertake this study, and for much valuable help and criticism in the preparation of the paper.

#### REFERENCES

- (1) *Callins, L. A., Litzenberg, J. C., and Plass, E. D.*: AM. J. OBST. & GYNEC. 22: 604, 1931. (2) *Daichman, I.*: AM. J. OBST. & GYNEC. 24: 127, 1932. (3) *Essen-Möller, Elis*: Acta obst. et gynec. Scandinav. 8: 103, 1929. (4) *Linden, Oskar*: Acta obst. et gynec. Scandinav. 8: 35, 1929. (5) *Meyer, Leopold*: Arch. di ostet. e ginec. 8: 264, 1916. (6) *Nixon, W. C. W.*: J. Obst. & Gynec. Brit. Emp. 38: 821, 1931. (7) *Ogata*: Beitr. zu Geburtsh. u. Gynäk. 1908. (8) *Peckham*: AM. J. OBST. & GYNEC. 22: 606, 1932. (9) *Quigley, James K.*: AM. J. OBST. & GYNEC. 21: 234, 1931. (10) *Richter and Hess*: Monatsschr. Geburtsh. u. Gynäk. 38: 1913. (11) *Schulze, Margaret*: J. A. M. A. 93: 824, 1929.

2 WEST EIGHTY-SEVENTH STREET

---

Smith, J.: A Further Investigation into the Source of Infection in Puerperal Fever, J. Obst. & Gynec. Brit. Emp. 40: 991, 1933.

In 41 cases of puerperal fever in which *Streptococcus hemolyticus* was isolated from the uterus, it was found that 32 of the patients were infected from a focus in the attendant and 9 from a focus in the patient herself. Of these 41 patients the source was traced to the throat or nose of the attendant in 31 instances and to the throat or nose of the patient in 8 instances. In 2 cases, 1 attendant and 1 patient, the source was a septic focus elsewhere in the body.

WILLIAM F. MENGERT.

# THE EFFECT OF ADMINISTRATION OF PREPARATIONS OF GROWTH HORMONE OF THE ANTERIOR LOBE OF THE PITUITARY UPON GESTATION AND THE WEIGHT OF THE NEWBORN (ALBINO RATS)\*

RUTH M. WATTS, M.S., PH.D., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, the University of Chicago)*

THE consideration of the interrelationship of the pituitary and pregnancy brings into question the influence of the hormones of the anterior pituitary upon the course of pregnancy and the development of the young. The present report is a study of the effect of the growth hormone of the anterior lobe upon the maternal weight changes of the albino rat during gestation and upon the weight of the newborn young. The problem has been undertaken at the suggestion of Dr. Fred L. Adair.

Teel, 1926,<sup>6</sup> treated pregnant rats with an alkaline extract of the anterior lobe. This extract was potent in growth hormone but it contained appreciable amounts of a factor which caused luteinization of the ovary and inhibition of estrus. Administration of this extract to pregnant rats prolonged the gestation period from two to six days and interfered with normal parturition. Treatment throughout pregnancy invariably resulted in stillborn young of greater than normal size.

Hain, 1932,<sup>2, 3</sup> confirmed these results and in addition, treated 6 pregnant rats with a more highly purified preparation made according to the method of Van Dyke and Wallen-Lawrence.<sup>7</sup> With the exception of two rats which received hormone treatment only on the fifth and sixth days of pregnancy, the results were similar to those reported for the crude extract. In 1934, Hain<sup>4</sup> extended the work to include ovariectomized pregnant rats. Neither the alkaline extract nor Phynone (growth hormone, The Wilson Laboratories) prolonged gestation in the absence of the ovaries.

Sontag and Munson, 1934,<sup>5</sup> administered antuitrin-G (growth hormone, Parke, Davis and Co.) to twelve pregnant rats. These workers reported prolongation of gestation and young which were heavier than the controls and which were often stillborn.

In the present investigation, growth hormone preparations have been made from beef anterior lobes according to the method of Van Dyke and Wallen-Lawrence.<sup>7</sup> Some preparations when administered to pregnant rats prolonged gestation and interfered with normal parturition; other preparations permitted normal delivery at term. It has been concluded that the growth hormone is not responsible for prolongation of gestation observed with some preparations. The young of normal term development have been found to be heavier than the controls.

\*This work has been conducted under a grant from The Douglas Smith Foundation for Medical Research of the University of Chicago. The writer is indebted to Emphila M. Fisher for technical assistance.

This paper was presented in part at the meeting of the American Society of Biological Chemists, Detroit, April 13, 1935.

*Selection of Animals.*—Albino rats of the University of Chicago Wistar strain were employed in this study. Young rats with a history of one normal litter were used for the preliminary work but a more detailed standardization was necessary for the later work. The animals weighed from 170 to 200 gm. at the beginning of the first pregnancy. Chart 1 shows that at this weight the females of this colony have reached the weight plateau and are thirteen to eighteen weeks of age. In this later work, hormone preparations were administered only during the second pregnancy. Only those rats were treated which had a first pregnancy history of a gestation period of twenty-one or twenty-two days with normal parturition, and which produced first litters of four or more young with a mean weight per litter within the range of 4.5 to 5.4 gm.

*Methods of Breeding.*—Group breeding was employed. The animals were mated at 5 P.M. and the vaginal spread was examined for sperm before 9 A.M. of the following day. The day sperm was found was called day 1 and the preceding day,

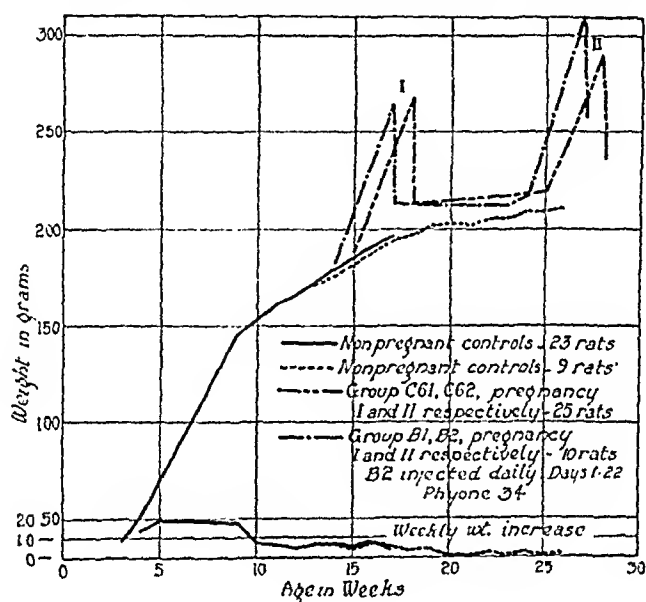


Chart 1.

day 0. The rats were kept in individual cages during gestation and lactation. They were allowed to rest three weeks before the next gestation period.

*Weighings.*—All maternal weights were taken in the morning before the daily feeding. The rats were weighed either daily or on days 0, 1, 5, 10, 21, 22, post-partum, at the end of the lactation period, and weekly until the next gestation period.

The newborn young were weighed individually as soon after birth as possible. A record was kept of the hour of birth and as to whether or not the young had suckled before the weight was taken.

*Diet.*—The rats received a constant diet consisting of yellow corn meal (whole corn), alfalfa, linseed meal with oil, casein, calcium carbonate, sodium chloride, whole milk and bread, supplemented twice weekly by lettuce and ground beef.

*Growth Hormone Preparations.*—Growth hormone preparations were made from anterior lobes of beef pituitary glands according to the method of Van Dyke and Wallen-Lawrence.<sup>7</sup> The anterior pituitary glands from which extracts were made in this laboratory and all other preparations were kindly furnished by Dr. David



Klein of The Wilson Laboratories. Early preparations contained a substance which prolonged the gestation period and interfered with normal parturition but later preparations were free from this factor.

*Assay of Growth Hormone Preparations.*—All preparations were assayed in this laboratory according to the method of Van Dyke and Wallen-Lawrence.<sup>7</sup> Dilutions of growth hormone preparations were used which caused a 3 to 4 per cent increase in the weight of the injected group (10 female rats) over the control group in a three-day injection period.

*Injection Method.*—Growth hormone preparations were injected subcutaneously daily during the experimental period. The dose was proportioned to body weight throughout the injection period.

*Statistical Interpretation.*—The significance of the mean values of the various control and experimental groups has been tested by the *t*-test method recommended by Fisher<sup>1</sup> for the comparison of small groups. The value "P" is the probability that the means compared could have been obtained by random sampling of the same population. For example,  $P = 0.01$  signifies that there is one chance per 100 that the mean values from which this probability was computed could have been obtained without any treatment, by merely drawing another sample from the control group. The probability of 0.01 or 0.02 has been considered to show significant difference in the means. Values are expressed in terms of the standard error.

#### CONTROL GROUPS

Control groups have been compiled for comparison of maternal weight changes during gestation or for weights of newborn young or both. Since it is desirable in comparison of these values to know the number of the pregnancy or litter, the data have been arranged according to these numbers. In a series of 500 normal pregnancies in this colony, only 75 rats were followed throughout their first two pregnancies. Consequently, some of the rats appear in more than one control group. For example, Group C 61 was selected from Group C 21 to fit experimental Group B 1 in which the number per litter was larger. Within each group, the same rats appear in the first and second pregnancies, e.g., in Groups C 21 (first pregnancy) and C 22 (second pregnancy).

It is difficult to affix definite standards for maternal weight changes because the female rat never attains complete growth stasis. The weight changes are complicated further by the fact that there is a permanent weight increase due to pregnancy (see Chart 1).

Standardization of the litter values has been attempted by excluding litters with less than four young and by discarding rats which produced first litters in which the mean weight of young has fallen outside the range of 4.5 to 5.4 gm.

#### SELECTION OF STANDARDS

1. *Term.*—In a series of 328 pregnancies timed from the finding of sperm in the vaginal spread, delivery occurred on the twenty-second day in 236 cases (87.2 per cent), on the twenty-third day in 38 cases (11.6 per cent) and at other times in 4 cases (1.2 per cent). In this work delivery on the twenty-second or twenty-third day has been considered normal.

2. *Number of Young Per Litter.*—For purposes of standardization litters of less than four have been excluded from all groups. Consideration of 114 first litters and 53 second litters showed that 96.5 per cent and 96.2 per cent, respectively, of these litters had more than four young per litter.

3. *Mean Weight of Young Per Litter.*—General observation of a large series of consecutive litters indicated that each rat tends to produce young of the mean weight for the colony. A rat which produces a first litter with a mean weight of young near that of the colony will tend to produce a second litter with the mean weight of the young within the same range. If the first litter is far removed from this range the second litter will bear no definite relation to the first litter but will tend to approach the mean for the colony.

To test the validity of this observation, a group of 57 rats which produced first and second litters with more than 3 young was analyzed. In this work the "normal" range of the mean weight of young per litter has been arbitrarily selected as 4.5 to 5.4 gm. Forty-five rats (78.9 per cent) produced first litters with the mean weight of young within the range 4.5 to 5.4 gm. and 12 rats (21.1 per cent) produced young with a mean weight outside this range. Of the 45 rats which produced young within this range in the first litter, 34 rats (75.6 per cent) produced second litters with young within this same range, 5 rats (11.1 per cent) exceeded this range by  $\pm 0.1$  gm. and 6 rats (13.3 per cent) fell definitely outside the range.

Comparisons of the mean weight of young of second litters of different groups have been considered most reliable when this type of selection has been employed for first litters in both the control and experimental groups. Only rats which produced first litters with a mean weight within the range 4.5 to 5.4 gm. have been used for experimental purposes in their second pregnancies. This type of selection in the first pregnancy does not affect the mean weight of the young of the second litter. For example, the mean weight of the young of Group C 62 (selected rats) was 5.13 gm. and of group B 42 (unselected rats), 5.11 gm. These values are in Table IV.

#### THE EFFECT OF AGE AND SUCKLING UPON THE WEIGHT OF NEWBORN YOUNG

It has been reported that the weights of newborn rats are in error because the young have suckled before the weights were taken. In this work a record was kept for each newborn rat as to whether or not it had suckled before the weight was taken. Since it is often difficult to obtain weights before the young have suckled, two control groups were compiled to show the possible discrepancy in weight from this source.

In the first group the young of 44 litters were weighed at birth before suckling and then at various hours of age after suckling. These data are shown in Table I. Until after eight hours of age the mean weight of young per litter did not change. For example, the mean weight of the young of 10 litters was  $5.15 \pm 0.15$  gm. at birth and  $5.14 \pm 0.13$  gm. at eight hours of age. This constancy in weight exists for each litter as well as for a group of litters.

TABLE I. EFFECT OF AGE UPON WEIGHT OF NEWBORN RATS

NO. OF LITTERS	MEAN WEIGHT (GRAMS) OF NEWBORN YOUNG PER LITTER $\pm$ STANDARD ERROR				
	SUCCESSIVE HOURS OF AGE				
	0	5	7	8	14-16
22	$5.12 \pm 0.09$	$5.14 \pm 0.09$			
8	$4.99 \pm 0.08$		$4.99 \pm 0.07$		
10	$5.15 \pm 0.15$			$5.14 \pm 0.13$	
4	$5.27 \pm 0.14$				$5.47 \pm 0.23$

The second group consists of 44 second litters, compiled according to whether or not the young had suckled before the weights were taken; the young of 9 litters (C 32+) had suckled and those of 35 litters (C 32-) had not. The data are shown in Table II. The mean weight of young for the entire group (C 32) was  $5.14 \pm 0.06$

TABLE II. EFFECT OF AGE UPON WEIGHT OF NEWBORN RATS

GROUP NO.	PREG-NANCY NO.	NO. OF LITTERS	SUCKLED	NO. OF YOUNG PER LITTER $\pm$ STANDARD ERROR	MEAN WEIGHT (GM.) OF YOUNG PER LITTER $\pm$ STANDARD ERROR	LITTER WEIGHT (GM.) $\pm$ STANDARD ERROR
C 32+	2	9	+	$9.8 \pm 0.5$	$5.26 \pm 0.08$	$51.28 \pm 2.33$
C 32-	2	35	-	$8.0 \pm 0.3$	$5.12 \pm 0.07$	$40.75 \pm 1.68$
C 32	2	44	$\pm$	$8.4 \pm 0.3$	$5.14 \pm 0.06$	$42.91 \pm 1.56$

gm., for the suckled group (C 32+),  $5.26 \pm 0.08$  gm., and for the group not suckled (C 32-),  $5.12 \pm 0.07$  gm. Comparison of the mean weight of the young of the suckled and not suckled groups gives a probability of 0.33. Since some of the young appearing in Group C 32+ were of a maximum age considered as newborn and since experimental young were never as old as these when weighed and many had not suckled, the discrepancy in weight due to suckling has been considered negligible.

## EFFECT OF NUMBER PER LITTER ON THE WEIGHT OF THE YOUNG

In order to ascertain the extent to which the number of young per litter influences the mean weight of the young, 114 first litters and 53 second litters have been arranged according to the number of young per litter. These values appear in Table III. None of the young had suckled. Except for extremes of number, the mean weight of young

TABLE III. EFFECT OF NUMBER PER LITTER ON WEIGHT OF NEWBORN RATS\*

NO. OF RATS PER LITTER	FIRST LITTERS			SECOND LITTERS		
	NO. OF LITTERS	MEAN WEIGHT OF YOUNG $\pm$ STANDARD ERROR	LITTER WEIGHT $\pm$ STANDARD ERROR	NO. OF LITTERS	MEAN WEIGHT OF YOUNG $\pm$ STANDARD ERROR	LITTER WEIGHT $\pm$ STANDARD ERROR
		GM.	GM.		GM.	GM.
1	1	6.2	6.2	1	6.6	6.6
2	0			0		
3	3	$5.67 \pm 0.19$	$16.93 \pm 0.54$	1	5.5	16.5
4	3	$5.73 \pm 0.19$	$22.80 \pm 0.70$	5	$5.48 \pm 0.30$	$21.88 \pm 1.16$
5	8	$5.55 \pm 0.31$	$27.75 \pm 1.53$	3	$5.43 \pm 0.19$	$27.10 \pm 0.99$
6	6	$5.05 \pm 0.14$	$30.27 \pm 0.84$	3	$5.17 \pm 0.22$	$31.00 \pm 1.39$
7	18	$5.05 \pm 0.09$	$35.35 \pm 0.60$	9	$5.28 \pm 0.10$	$37.01 \pm 0.66$
8	21	$5.10 \pm 0.07$	$40.80 \pm 0.58$	12	$5.21 \pm 0.12$	$41.63 \pm 0.96$
9	17	$5.11 \pm 0.11$	$46.12 \pm 1.02$	9	$4.90 \pm 0.11$	$44.08 \pm 1.00$
10	16	$4.86 \pm 0.07$	$48.54 \pm 0.69$	5	$5.22 \pm 0.05$	$52.26 \pm 0.40$
11	14	$4.98 \pm 0.08$	$54.78 \pm 0.93$	3	$4.73 \pm 0.10$	$52.13 \pm 1.19$
12	5	$4.86 \pm 0.12$	$58.24 \pm 1.29$	0		
13	2	3.5 & 5.1	45.1 & 66.5	1	4.8	62.2
14	0			1	4.9	68.0
Total	114			53		
Mean of Group	8.3	$5.09 \pm 0.05$	41.69	7.7	$5.20 \pm 0.06$	39.32

\*None of these rats had suckled.

remains fairly constant irrespective of the number of young per litter. The litter weight increases progressively with the increase in the number in the litter. The calculated and observed values for the mean weights of young and the mean litter weights are presented graphically in Chart 2.

*Method of Breeding.*—It was suggested that selective breeding might produce young of more uniform weight than group breeding. Pregnancies 1 and 2 for a selective breeding group, in which each female was mated with the same male in two consecutive pregnancies, are represented as Groups D 11 and D 12, respectively; for a group breeding group as C 21 and C 22, respectively. These data were selected in regard to normal pregnancy history, litters of 4 or more young in both pregnancies and the mean weight of the young for the first litter within the range 4.5 to 5.4 gm. The mean weight of the young per litter for the selective breeding group was  $5.08 \pm 0.07$  and  $5.18 \pm 0.09$  gm. for the first and second litters, respectively; comparison gives a probability of 0.40. The mean weight of the young per litter for

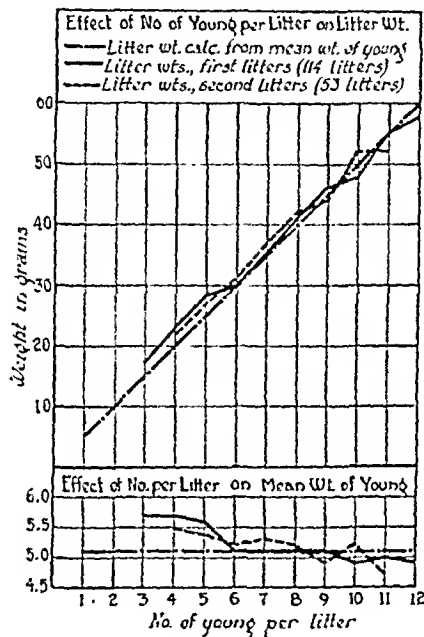


Chart 2.

the group breeding group was  $5.06 \pm 0.04$  gm. and  $5.13 \pm 0.07$  gm. for the first and second litters, respectively; comparison gives a probability of 0.43. Since the probability of significant difference in means is of the same magnitude for both groups, the method of breeding has not been considered to be a significant factor when a group of animals is used. These values are shown in Table IV. Better agreement was obtained between the mean weights of the young of the first and second litters of individual rats in the selective breeding group than in the group breeding group but the values were not uniform enough to justify comparison of the litters of individual animals.

*Consecutive Pregnancy and Litter Values.*—The number of the pregnancy or of the litter influences the value obtained. A group of 16 rats was followed through the first three consecutive pregnancies, represented as Groups B 41, B 42, B 43, respectively, in Table IV. In each case the gestation period and parturition were normal and each litter contained more than 3 young.

The maternal weight changes were greater in the first pregnancy than in the second or third. The mean maternal weight increases during 3 consecutive gestation

TABLE IV. COMPARISONS OF CONSECUTIVE PREGNANCIES AND LITTERS

GROUP NO.	PREG. NO.	NO. IN GROUP	SELECTION		MATERNAL WEIGHT INCREASE						NO. OF YOUNG PER LITTER $\pm$ STANDARD ERROR	MEAN WEIGHT OF YOUNG $\pm$ STANDARD ERROR	LITTER WEIGHT $\pm$ STANDARD ERROR
			NO. PER LITTER	MEAN WEIGHT OF YOUNG	DAY 0-22		DAY 0-P.P.		PER $\pm$ STANDARD ERROR	PER CENT			
					INCREASE $\pm$ STANDARD ERROR	GM.	INCREASE $\pm$ STANDARD ERROR	GM.					
C 21	1	29	> 3	GM. 4.5-5.4	81.74 $\pm$ 3.30	43.6	26.62 $\pm$ 2.14	14.2	8.8 $\pm$ 0.3	GM. 5.06 $\pm$ 0.04	GM. 44.19 $\pm$ 1.61		
C 22	2	29	> 3	-	72.06 $\pm$ 2.09	32.5	17.03 $\pm$ 1.91	7.7	8.4 $\pm$ 0.4	5.13 $\pm$ 0.07	42.91 $\pm$ 1.92		
C 61	1	25	6-11	4.5-5.4	79.07 $\pm$ 2.84	42.2	25.58 $\pm$ 2.21	13.7	8.5 $\pm$ 0.3	5.05 $\pm$ 0.05	42.92 $\pm$ 1.28		
C 62	2	25	> 3	-	70.59 $\pm$ 2.26	32.3	17.10 $\pm$ 2.03	7.8	8.2 $\pm$ 0.4	5.12 $\pm$ 0.09	41.47 $\pm$ 2.03		
C 81	1	14	6-9	5.1-5.4					8.1 $\pm$ 0.3	5.23 $\pm$ 0.02	42.67 $\pm$ 1.48		
C 82	2	14	> 3	-					7.6 $\pm$ 0.6	5.26 $\pm$ 0.12	39.31 $\pm$ 2.75		
C 31	1	44	> 3	4.5-5.4					8.8 $\pm$ 0.3	5.01 $\pm$ 0.04	43.92 $\pm$ 1.42		
C 32	2	44	> 3	-					8.4 $\pm$ 0.3	5.14 $\pm$ 0.06	42.91 $\pm$ 1.56		
C 41	1	41	> 3	-	80.20 $\pm$ 2.68	42.9	28.03 $\pm$ 2.04	15.0					
C 42	2	41	> 3	-	71.80 $\pm$ 2.18	32.6	19.43 $\pm$ 1.78	8.4					
D 11	1	12	> 3	4.5-5.4									
D 12	2	12	> 3	-					9.7 $\pm$ 0.4	5.08 $\pm$ 0.07	48.98 $\pm$ 2.15		
B 41	1	16	> 3	-	80.89 $\pm$ 5.33	42.7	23.91 $\pm$ 3.48	12.6	9.4 $\pm$ 0.5	5.18 $\pm$ 0.09	48.63 $\pm$ 2.85		
B 42	2	16	> 3	-	71.26 $\pm$ 3.63	32.3	16.10 $\pm$ 3.04	7.3	8.6 $\pm$ 0.5	5.16 $\pm$ 0.09	43.98 $\pm$ 2.35		
B 43	3	16	> 3	-	70.97 $\pm$ 4.32	31.1	19.68 $\pm$ 3.26	8.6	8.6 $\pm$ 0.4	5.11 $\pm$ 0.09	43.80 $\pm$ 2.06		
									7.8 $\pm$ 0.5	5.36 $\pm$ 0.06	41.40 $\pm$ 2.64		

periods (day 0-22) were 80.89, 71.26, 70.97 gm. or increases of 42.7 per cent, 32.3 per cent, and 31.1 per cent, respectively. A similar difference was found in the permanent gain represented by the increase from day 0 to postpartum (P.P.). A small part of these gains can be attributed to the slope of the normal weight curve and the other part to the effect of pregnancy upon the weight curve. The normal weight curve and pregnancy curves of the first two pregnancies of similar Groups C 61 and C 62, are shown in Chart 1. Comparisons of maternal weight changes of the first pregnancy with those of the second or third are not considered reliable.

Slight differences due to the number of the litter were noted in the litter values. For example, the mean weights of the young for the first, second, and third litters were 5.16, 5.11, 5.36 gm., respectively. Comparisons of values of first and second litters are considered most trustworthy.

*Comparison of First and Second Pregnancies and Litters.*—After a consideration of the values obtained in a study of three consecutive pregnancies (Groups B 41, B 42, B 43) only the first two pregnancies were used for control and experimental purposes. The first pregnancy served as a preliminary control and the second for a final control group, or for experimental use. Table IV shows several groups compiled from one large group for various control purposes.

Comparison of maternal weight changes should be made between groups of the same pregnancy number. Within groups of the same number the agreement is good. For example, the increases in the mean maternal weight during gestation (day 0-22) for Groups C 22, C 62, C 42, were 72.06, 70.59, 71.80 gm., or 32.5 per cent, 32.3 per cent, and 32.6 per cent, respectively.

Comparisons of litter values are most trustworthy when litters of the same number are considered. For example, the mean weights of the young of the second litters of Groups C 22, C 62, and C 32 were 5.13, 5.12, and 5.14 gm., respectively. However, comparison of the values of the first litter with those of the second may serve as a second check in comparisons of the mean weight of the young. For example, the mean weights of the young of the first litters, Group C 21, and second litters, Group C 22, were 5.06 and 5.13 gm., respectively. Differences of this magnitude, considered statistically, are not significant.

#### THE EFFECT OF GROWTH HORMONE ON GESTATION AND BIRTH WEIGHT

*I. Preliminary Work.*—In the preliminary work, growth hormone preparations were administered daily for various periods to 42 pregnant rats with histories of at least one normal litter. Some of the preparations prolonged gestation, interfered with normal parturition, and resulted in stillborn young; other preparations did not exhibit these detrimental effects. The preparations which prolonged gestation did not inhibit the estrus cycle of the normal rat but did tend to prolong the estrus phase. Lactation was not impaired. The preparations which prolonged gestation continued to exert an effect in the subsequent pregnancy. This effect was marked by slight prolongation of gestation, protracted parturition and young of increased size.

Seventeen rats received preparation No. 32 (Phyone, The Wilson Laboratories) from the seventh to the fourteenth day of pregnancy to delivery. This preparation caused prolongation of gestation from two to five days. The mean weight of the young per litter ranged from 5.5

to 7.1 gm. with young as large as 8.6 gm. The young were often still-born and macerated at delivery. Because of the macerated condition of the young, the data on the weights were incomplete and statistical consideration was impossible. Since prolongation of gestation produced by other means has been reported to result in young of increased size no significance has been placed in the increase in weight of young of over-term development. The maternal weight changes were significant but the varying periods of injection made statistical study undesirable. The findings were similar to those reported by Teel, Hain, and Sontag and Munson.

Autopsy or cesarean section was performed on animals treated with preparations which prolonged gestation. One or two days after normal term, the young were often living and were larger than normal; the placentas were slightly or almost completely detached. Autopsy at later times showed completely dislodged placentas, dead fetuses, and marked resorption.

Various preparations made in this laboratory showed that prolongation of gestation with interference with normal parturition was not a property of the growth hormone but of some factor contaminating it. Twenty-five rats received these various preparations but only four of this group which had normal gestation and parturition were injected for periods suitable for statistical study. These are represented as Group E 2 in Tables V and VI. The maternal weight changes were significant. The mean weight of the young per litter was  $5.90 \pm 0.11$  gm. for Group E 2 and  $5.12 \pm 0.09$  gm. for control Group C 62. Statistical comparison of these values gives  $P = 0.0005$ , a probability of 1 chance in 2,000 that these values could have been obtained by random sampling of the control population.

II. *Later Work.*—Preparations of growth hormone which did not prolong gestation or interfere with normal parturition are considered in this section. These preparations had no influence upon subsequent pregnancies. In each group the rats weighed 170 to 200 gm. at the beginning of their first pregnancies. The first pregnancy was used for a preliminary control; the second was used for experimental purposes.

*Group A.*—Eight rats received growth hormone preparation No. 23 (Phyone, The Wilson Laboratories) daily from the tenth or twelfth day of the second pregnancy to delivery. For each rat the mean weight of the young per litter was greater than that of the preceding litter and greater than the mean for either the first or the second litters of the controls.

Four of this group which were injected for comparable periods are considered as Group A 2. The mean maternal weight increase during gestation was 106.13 gm. (46.6 per cent) for Group A 2 and 70.59 gm. (32.3 per cent) for the control Group C 62. The mean permanent gain was 44.40 gm. (19.5 per cent) for the injected Group A 2 and 17.10 gm. (7.8 per cent) for the control Group C 62. The mean weight of young per litter for Group A 2 was  $5.70 \pm 0.06$  gm.; for the control Group C 62,  $5.12 \pm 0.09$  gm.; and for Group A 1 (first litter),  $5.18 \pm 0.11$  gm. Statistical

TABLE V. EFFECT OF PIYONE ADMINISTRATION ON MATERNAL AND NEWBORN WEIGHTS

GROUP NO.	PREG. NANCY NO.	NO. IN GROUP	PHYONE ADMINISTRATION		MATERNAL WEIGHT INCREASE				NO. OF YOUNG PER LITTER $\pm$ STANDARD ERROR	MEAN WEIGHT OF YOUNG $\pm$ STANDARD ERROR	LITTER WEIGHT $\pm$ STANDARD ERROR
			PREPARATION NO.	DAYS OF PREG.	DAY 0-22		DAY 0-P.P.				
					INCREASE $\pm$ STANDARD ERROR	PER CENT	INCREASE $\pm$ STANDARD ERROR	PER CENT			
C 61	1	25	Control	-	GM. 79.07 $\pm$ 2.84	42.2	GM. 25.58 $\pm$ 2.21	13.7	GM. 8.5 $\pm$ 0.3	5.05 $\pm$ 0.05	42.92 $\pm$ 1.28
C 81	1	14	Control	-	-	-	-	-	8.1 $\pm$ 0.3	5.23 $\pm$ 0.02	42.67 $\pm$ 1.48
A 1	1	4	Control	-	-	-	-	-	11.3 $\pm$ 0.7	5.18 $\pm$ 0.11	57.98 $\pm$ 3.06
B 1	1	10	Control	-	81.32 $\pm$ 5.82	44.6	31.00 $\pm$ 2.78	17.0	8.3 $\pm$ 0.4	5.13 $\pm$ 0.08	42.56 $\pm$ 2.50
P 1	1	9	Control	-	82.41 $\pm$ 5.11	43.3	27.43 $\pm$ 4.68	14.4	7.6 $\pm$ 0.3	5.24 $\pm$ 0.04	39.68 $\pm$ 1.53
C 62	2	25	Control	-	70.59 $\pm$ 2.26	32.3	17.10 $\pm$ 2.03	7.8	8.2 $\pm$ 0.4	5.12 $\pm$ 0.09	41.47 $\pm$ 2.03
C 82	2	14	Control	-	-	-	-	-	7.6 $\pm$ 0.6	5.26 $\pm$ 0.12	39.31 $\pm$ 2.75
E 2	2	4	No. 42	10-22	92.58 $\pm$ 6.23	42.3	35.50 $\pm$ 6.73	16.2	9.8 $\pm$ 0.4	5.90 $\pm$ 0.11	57.68 $\pm$ 2.60
A 2	2	4	No. 23	10-22	106.13 $\pm$ 5.39	46.6	44.40 $\pm$ 4.56	19.5	10.3 $\pm$ 0.7	5.70 $\pm$ 0.06	58.23 $\pm$ 4.02
B 2	2	10	No. 34	1-22	93.30 $\pm$ 4.48	43.1	40.39 $\pm$ 4.24	18.7	8.6 $\pm$ 0.5	5.52 $\pm$ 0.13	47.14 $\pm$ 2.72
P 2	2	9	No. 34	10-22	94.29 $\pm$ 2.57	43.6	46.06 $\pm$ 3.65	21.3	7.3 $\pm$ 0.4	5.83 $\pm$ 0.10	42.46 $\pm$ 2.08



comparison of the mean weight per litter of Groups A 2 and C 62 gives a probability of 0.009. Therefore the increase in the weight of the young may be considered significant. These values are found in Tables V and VI.

TABLE VI. PROBABILITY VALUES

GROUPS COMPARED	PREG-NANCY NUMBER	PHYONE ADMIN.	PROBABILITIES THAT THE DIFFERENCES IN MEANS ARE DUE TO RANDOM SAMPLING					
			MATERNAL INCREASE		NEWBORN YOUNG			
			DAY 0-22	DAY 0-P.P.	NO. OF YOUNG PER LITTER	WEIGHT OF YOUNG		LITTER WEIGHT
						PER LITTER	PER GROUP	
E 2 vs. C 62	2, 2	+, -	0.000,6	0.002	0.12	0.0005	0.000,000	0.003
A 2 vs. C 62	2, 2	+, -	0.000,000	0.000,001	0.05	0.009	0.000,000	0.002
B 2 vs. C 62	2, 2	+, -	0.000,001	0.000,000	0.58	0.01	0.000,000	0.13
P 2 vs. C 62	2, 2	+, -	0.000,000	0.000,000	0.22	0.000,009	0.000,000	0.79
P 2 vs. C 82	2, 2	+, -			0.71	0.002	0.000,000	0.43

*Group B.*—Growth hormone preparation No. 34 (Phyone, The Wilson Laboratories) was administered daily to 12 rats from the first day to the end of the second pregnancy. Of this group, 1 rat had a litter of 3, 1 went slightly overterm, and 10 are considered as Group B. Pregnancies 1 and 2 of this group are represented as Groups B 1 and B 2, respectively, in Tables V and VI.

The mean weight increase during gestation was 93.30 gm. (43.1 per cent) for Group B 2 and 70.59 gm. (32.3 per cent) for the control Group C 62. The mean permanent increase was 40.39 gm. (18.7 per cent) for Group B 2 and 17.10 gm. (7.8 per cent) for control Group C 62. These increases in maternal weight are significant. They are shown graphically in Chart 2.

The mean weight of the young was  $5.52 \pm 0.13$  gm. for the injected Group B 2,  $5.12 \pm 0.09$  gm. for the control Group C 62 and  $5.13 \pm 0.08$  gm. for Group B 1 (first litter of the experimental group). The increase in the mean weight of the young of the injected Group B 2 over the control Group C 62 was 0.40 gm. (7.8 per cent) and of the injected group over the first litter of the experimental group was 0.39 gm. (7.6 per cent). The increase in the mean weight of the young of the second litter over the first litter of the controls (Groups C 61, C 62) was 0.07 gm. (1.4 per cent). The mean of the weights of the largest newborn rat of each litter of the control Group C 62, was 5.7 gm. and the mean weight of the smallest was 4.4 gm.; in the injected Group B 2 the corresponding values were 6.1 and 4.9 gm. This increase in the weight of the young is of the nature of uniformly larger young. The mean weight of the young for each group has been calculated from the mean weights of the young per litter and also from the individual weights of the young in each group. The significance of the differences in the mean weight of the young of B 2 (injected) and C 62 (control), calculated from the means of the litters, gives  $P = 0.01$  and, calculated from the individuals in the group, gives  $P = 0.000,000$ . This increase in the weight of the young has been considered significant. The values are found in Table V and statistical comparisons in Table VI.

*Group P.*—Growth hormone preparation No. 34 (Phyone, The Wilson Laboratories) was administered daily to eleven rats from the tenth day to the end of the second pregnancy. Nine of these are considered as Group P; pregnancies one and two are represented as Groups P 1 and P 2 respectively, in Tables V and VI.

The maternal weight change during gestation and the permanent weight change show a significant increase; the mean maternal weight change for Group P 2 during

gestation was 94.29 gm. (43.6 per cent) and for Group C 62, 70.59 gm. (32.3 per cent). The mean permanent gain for P 2 was 46.06 gm. (21.3 per cent) and for C 62, 17.10 gm. (7.8 per cent).

The mean number of young per litter was 7.3 for Group P 2 and 8.2 for the control Group C 62. Consequently, control Groups C 81 and C 82 were selected to fit this experimental group. The mean number of young of Group C 82 was 7.6.

The mean weight of young per litter was  $5.83 \pm 0.10$  for Group P 2,  $5.12 \pm 0.09$  for Group C 62,  $5.26 \pm 0.12$  for Group C 82, and  $5.24 \pm 0.04$  for Group P 1. The increase in the weight of the young of the injected Group P 2 over the control group C 62 was 0.71 gm. (13.9 per cent); the increase over Group C 82 was 0.57 gm. (10.8 per cent); the increase over Group P 1 was 0.59 gm. (11.3 per cent). The increase of the mean weight of the young of C 62 over C 61 was 0.07 gm. (1.4 per cent). The mean of the weights of the largest rat in each litter of Group P 2 was 6.3 gm. and of the smallest, 5.2 gm.; for Group C 62 these values were 5.7 and 4.4 gm. Statistical comparison of the mean weights of the young of Groups P 2 and C 82 gives  $P = 0.002$  when calculated from the mean weights of young per litter and  $P = 0.000,000$  when calculated from the individual weights of the young in the group. This increase in weight is considered significant.

#### SUMMARY

1. Control groups have been compiled to show (1) the effect of the number of the pregnancy upon the maternal weight changes during pregnancy and upon the weight of the newborn, (2) the effect of age and suckling upon the weight of the newborn, (3) the effect of the number per litter upon the mean weight of the newborn, and, (4) the effect of the method of breeding upon the mean weight of the newborn.

2. Preparations of the growth hormone of the anterior lobe of the pituitary have been administered daily to pregnant rats for varying periods and in amounts which caused an average daily increase of 1 per cent in nonpregnant rats. Some preparations prolonged gestation, interfered with normal parturition and resulted in stillborn young as reported by other workers. Other preparations did not exhibit these effects. It has been concluded that the growth hormone itself is not responsible for these effects. The increases in the maternal weight changes during gestation were significant. The weight of the newborn young delivered at term was greater in the injected groups than in the control group. These differences, considered statistically, are significant.

I wish to express my appreciation to Dr. Fred L. Adair for his consultation and advice during the course of this investigation.

#### REFERENCES

- (1) Fisher, R. A.: *Statistical Methods for Research Workers*, ed. 4, Edinburgh, 1932. Oliver and Boyd, p. 114. (2) Hain, A. M.: *Quart. J. Exper. Physiol.* 22: 71, 1932. (3) *Idem.*: 22: 249, 1932. (4) *Idem.*: 24: 101, 1934. (5) Sontag, L. W., and Munson, P. L.: *Am. J. Physiol.* 108: 593, 1934. (6) Tecl, H. M.: *Ibid.* 79: 170, 1926. (7) Van Dyke, H. B., and Wallen-Lawrence, Z.: *J. Pharmacol. & Exper. Therap.* 40: 413, 1930.

# HORMONIC INDUCTION OF MENSTRUATION IN AMENORRHEAS OF FROM THREE MONTHS' TO NINE YEARS' DURATION\*

CHARLES WILLIAM DUNN, M.D., PHILADELPHIA, PA.

(From the Abington Memorial Hospital, and St. Luke's and Children's Hospital)

ANY attempt to review the subject of the hormones concerned in the cyclic function of the ovary would necessitate a bibliography that extends into the hundreds or more of monographs and reviews on the subject, consequently citations will be restricted to those subjects which are intimately related to the administration of the hormones concerned in the text.

Allen and Doisy<sup>1</sup> in 1922 and 1924 applied the rodent vaginal smear studies of Stockard<sup>2</sup> (1917) to determine the presence of the female sex hormone and to standardize it. Butenandt<sup>3</sup> in 1929 and others isolated the female sex hormone in the pure crystalline state and determined its chemical formula.

Dodds and Robertson<sup>4</sup> in 1930 administered 10 M.U. of the female sex hormone daily to a series of cases for a period of three months and concluded: "The results do not at first sight indicate a very hopeful outlook for the use of this substance. Out of 80 odd cases treated, only 30 showed definite objective improvement, although practically all of them showed general improvement. . . . Much larger doses of the substance must be given before it is put aside as useless. A large series of cases should be treated with 50-100 units per day and with this very definite results might be obtained and many hundred units in a single dose will have to be tried before a definite answer can be given."

Parkes<sup>5</sup> in 1932 prophesied on a weight for weight basis that the human castrated female of 50 kg. would require 400,000 M.U. to induce a similar physiologic state as was induced in the experimental animal. This figure would not produce uterine growth in the human being.

Zondek in 1927 revealed the urine of pregnancy as a rich source of the female sex hormone; this opened up the field of research and made possible the work of Hildebrandt and Schwenk<sup>6</sup> in 1933 who, by a process of hydrogenation of the ketohydroxyestrin, were able to increase the estrin units in a gram from 8 to 30 million; thereby providing the large unit dosage. A later development from the same laboratory was the benzonation of the female sex hormone which permitted its gradual utilization by the body, in effect producing an "artificial ovary."

Mazer in 1933 determined that the benzonated hormone was excreted in the urine at a certain rate and was present in the urine on the fourth day following injection. His work was of great assistance and assurance to me in this study.

Zondek<sup>7</sup> in August of 1934 supplied the reason why results in the past were so baffling and discordant. He injected a total of 540,000 M.U. of follicular hormone into a (human) female and could only recover 3 per cent from the urine in fifteen days. In a human male he recovered only 5 per cent in ten days, following a single injection of 40,000 M.U.; and in a rat injected with 20,000 M.U. in a single dose

\*Read, by invitation, at meeting of the Obstetrical Society of Philadelphia, January 3, 1935.

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.

he obtained negative recovery from the urine. Zondek then injected similar large doses into a rat and killed it within three hours and extracted the whole animal and recovered less than 1 per cent; however, when he subjected the extracted material to hydrogenation he recovered 20 per cent of the female sex hormone. This conclusively demonstrated that the crystalline follicular hormone was rapidly inactivated in the body following its injection. Conducting similar experiments with the benzonated female sex hormone he found that it was not inactivated in the body of the rat.

The rôle of the anterior pituitary on the cyclic activity of the ovary is so well known that to state that it is the motor of the ovary appears sufficient.

Amenorrhea is of interest to the obstetrician and the gynecologist from a diagnostic as well as a therapeutic viewpoint. It is associated with constitutional and endocrine states, therefore therapy in amenorrhea is contingent upon the etiologic factor. The endocrine glands concerned in amenorrhea are the thyroid, the adrenal, the pituitary, and the ovary. Hyperfunction of the first two glands and hypofunction of the last two generally result in amenorrhea.

Kauffman<sup>8</sup> and Loeser<sup>9</sup> in 1933 demonstrated that by giving a series of injections of the benzonated female sex hormone (Progynon B) and then following with a series of the lutein hormone, that menstruation could be induced in the old and recent castrates. Kauffman<sup>10</sup> in 1934 has also administered large doses of the benzonated female sex hormone in cases of secondary amenorrhea and has induced menstruation.

In the cases to be reported we were dealing with a clinical syndrome that was a primary state to the patient and the amenorrhea was a secondary clinical phase. It was our belief that a deficit of the female sex hormone in the blood was the major factor responsible for the primary clinical state in four of the cases. The induction of menstruation was a secondary effect from the therapy, our prime purpose was to relieve the symptom complex.

CASE REPORTS

CASE 1.—Single, aged forty-two years. Type: nonobese, hypopituitary. Amenorrhea of three and one-half months associated with involutional melancholia.

*Clinical Symptoms:* Irritability, depression, psychic instability, self-destruction ideas, neuritis and weakness of upper extremities, headache, nausea, and vomiting.

*Menses:* Onset at fourteen years of age, regular, two days' duration and of scant amount. Aggravation of early migraine symptoms as menses diminished. Melancholia appeared with onset of amenorrhea in June, 1934.

*Genitals:* Labia small, uterus of the juvenile type, characterized by a long cervix and short body. The ovaries were small, hard and insensitive to firm palpation.

*Therapy:* One cubic centimeter of anterior pituitary liquid (Armour) every fifth day. (Previous ten weeks similar therapy without change in menses.) 10,000 R. U. progynon B (Benzonated female sex hormone\*) weekly with an occasional dose for early clinical symptoms.

\*I am indebted to Dr. Gregory Stragnell of the Schering Corporation for the supply of progynon B employed in this study.

*Results:* Menses began on September 12 and lasted five days with a good flow. Increase in the size of the uterus. Disappearance of melancholia and associated symptoms.

**CASE 2.**—Single, aged twenty-nine years. Amenorrhea of one year associated with obesity (186 pounds) of the hypopituitary type. The general body physique was short with the obesity existing about the trunk and with slight extension into the extremities. There was hyperextension of the elbows and a hard palatal deformity. The skin showed a tendency to purpura on slight blows.

*Clinical Symptoms:* Obesity began at the age of twenty years. During last two years she gained from 15 to 20 pounds. During the last year she has had headaches, nervous and vertigo spells, which last for two days each month.

*Menses:* Onset at the age of eleven years, irregular, duration two to three days and scant in amount. Last menses: October, 1933.

*Rectal Examination:* Uterus of the juvenile type and the external genitals were small. The breasts were large and pendulous but were chiefly fatty tissue.

*Laboratory:* Normal cholesterol and basal rate of minus 23. The patient, a nurse, stated that she had previously been given the following therapy for amenorrhea: 1 c.c. of antuitrin-S daily for four months, next two months antuitrin-S 1 c.c. daily and thyroid  $\frac{1}{4}$  grain t.i.d., next two months theclol capsule 1 t.i.d. and then 2 t.i.d., and the last therapy was antuitrin-S and ovarian substance 1 c.c. of each every second day for three months.

*Therapy:* On Nov. 3, 1934 she was put on the following therapy: 2 c.c. of the anterior lobe of the pituitary liquid every other day and 2,000 R.U. of progynon B every third day. She menstruated for the first time in over a year after one month of therapy on Dec. 8, 1934. Menses lasted seven days and were of moderate amount.

**CASE 3.**—Aged thirteen years. Onset of illness August, 1933. Amenorrhea of one year's duration associated with Simmond's disease.

*Clinical Symptoms:* Loss of weight of 52 pounds, hypotension, systolic pressure 75, diastolic pressure 50, vertigo, extreme mental and physical weakness, coldness of the extremities, melancholia, irritability, emotional outbreaks, rapid progression of symptoms, senile appearance, atrophy of the breasts and uterus.

*Menses:* Onset at the age of eleven and one-half years, regular, five days' duration and normal amount. Last menses: Aug. 16, 1933, aged twelve and one-half years.

*Rectal Examination:* Unsatisfactory, vaginal examination was required for differential diagnosis. Vaginal examination: uterus was markedly atrophic, felt as a small cylindrical mass and anatomical parts could not be differentiated. Vaginal cavity: mucous membrane dry.

*Laboratory:* X-ray of the chest and the Mantoux test negative. X-ray of pituitary fossa, negative. Mild degree of anemia. Basal metabolism rate minus 3.

*Therapy:* Two cubic centimeters of the anterior lobe of the pituitary (Armour) daily except Sunday and 10,000 R.U. of progynon B weekly for a period of three months. Progynon B continued weekly and the anterior lobe of the pituitary was gradually reduced to 2 c.c. weekly.

*Results:* Vaginal discharge began after the third week and appeared about twelve hours after each administration of progynon B. The discharge became more profuse and thickened and finally was bloody for four days (Aug. 16, 1934). Vaginal examination was made on August 16, and it was found that the uterus had increased in size about 300 per cent and the anatomical parts were now palpable.

Menses occurred the evening of the sixteenth and lasted one day followed by two days of bloody discharge; the next menses occurred October 1 and lasted three days, fair flow. Third period occurred on October 30 and lasted one day with two days of bloody discharge.

Her general improvement was evidenced by a normal mental state, gain in over 30 pounds, normal blood pressure, the hypertrophy of the breast and enlargement of the uterus.

CASE 4.—Married, aged forty-three years. Type: nonobese hypopituitary. Amenorrhea of nine years associated with status migraine.

*Clinical History:* Hypomenorrhea, hypogenitalia and sterility for twenty years. Migraine syndrome: thirteen years in monthly cycles. Menopause at thirty-four years, hot flashes, lack of libido, atrophy of the breasts.

*Laboratory:* Blood: female sex hormone, negative throughout the month. Anterior pituitary hormone positive throughout the month. Basal metabolism rate plus S. Blood chemistry, negative: Wassermann, negative.

*Therapy:* From June 22 to 29 she was given 160,000 R.U. of progynon B. In July, breast hypertrophy was evident. From July 27 to August 3 she was given 210,000 R.U. of progynon B with excellent clinical results. Four days later she had her first menstrual period in nine years and it lasted ten days. The breast hypertrophy was maintained. From September 1 to 6 she was given 400,000 R.U. of progynon B. On the seventh and last day she was given 90,000 R.U. to abort the attack which by its severity and course indicated a fifteen-day attack. (She had a 21-day attack in April, 1934.)

The breasts were hypertrophied to a degree that objectively and subjectively they were comparable to the postpartum engorged breasts, and consequently administration of the progynon B was stopped. The attack was aborted but residual symptoms persisted for seven days at which time the second menses came on and lasted five days and were of good amount. Although the patient experienced these attacks at least monthly she did not have an attack for seven weeks; in the meantime the breast hypertrophy had practically disappeared.

From October 21 to 26 she was given 280,000 R.U. of progynon B and a third menstrual period occurred five days later and lasted for ten days; however, the bleeding was intermittent after the fifth day.

*Results:* Three consecutive periods in a case of amenorrhea of nine years' duration. There were no toxic effects from the administration of 1,126,000 R.U. of progynon B in a period of one hundred and twenty-eight days. Single daily doses as high as 90,000 R.U. were given. Breast hypertrophy. Vaginal examination in November, 1934 revealed a normal sized uterus for her age of forty-three years. Clinical improvement and occasional control of symptoms.

CASE 5.—Married, aged twenty-six years. Amenorrhea of five and one-half months associated with a basophilic adenoma of the pituitary.

*Clinical Symptoms:* Obesity, regional; hypertrichosis, hypertension, headache, neuritis, pigmentation and striae, uterine hypoplasia and cystic ovaries. Optic changes. Abnormal growth of hair began at the age of thirteen years.

*Menses:* Onset at sixteen years, irregular, and lasted from one to three days and of diminished to scant amount. Pregnancy 1932; obesity began following pregnancy.

*Laboratory:* Wassermann and blood chemistry: negative. Basal metabolism rate plus 18. X-ray of pituitary: slight enlargement.

*Therapy:* Dosage of progynon B. 2,000 R.U. at variable periods depending upon clinical signs. Menstruated for one day on Oct. 26, 1934. Large dosage 5,000 to 10,000 weekly began in November and was increased to twice weekly with appear-

ance of vaginal discharge. This patient was given from December 11 to 27 a total of 80,000 R.U. of progynon B. No menses occurred and she was given 10 rabbit units of the luteohormone on December 29. Menses occurred on Dec. 31 and were still evident on Jan. 2, 1935 and the amount was of fair flow.

#### COMMENT

In the cases reported we were treating essentially a clinical syndrome; the failure of the ovarian function as well as altered function of the pituitary gland was an integral part of all. The pathology of the pituitary gland varies; in Simmond's disease we have atrophy, in the basophilic adenoma we have an adenoma of the pituitary gland and hyperplastic or adenomatous changes of the adrenal, in the status migraine and the involutional melancholia we have a pituitary gland which, to my way of interpreting the state, is secreting gonadotropic hormones but fails to find a receptive substance from or in the ovary, therefore we have a piling up of the prolans in the blood stream. In the case of amenorrhea and obesity we have a hypofunction of the pituitary.

In the case of the involutional melancholia, previous administration of the anterior lobe was not sufficient to improve the menses, but the addition of the progynon B brought about the first normal period.

In the hypopituitary obesity case, pituitary and pituitary-like preparations had been tried with no effect and the addition of the female sex hormone brought about menses. In the case of Simmond's disease the effectiveness of this combination is again manifested and it appears that it materially reduced the quantity of the benzonated female sex hormone required to be administered.

In the case of the basophilic adenoma we are confronted with a pituitary gland that we know to be in a state of basophilic hyperfunction, further they may give a positive pregnancy test.<sup>13</sup> It is a dangerous state and therefore the administration of the pituitary is contraindicated. The administration of progynon B for the associated clinical symptoms, however, produced menses after an amenorrhea of five months.

In the status migraine our blood determinations had shown that there was an excess of the prolan factor. This is a problem case and, as the work of Mazer had shown that elimination was rapid, I felt justified in pouring in the benzonated sex hormone. Furthermore, during pregnancy large amounts are tolerated. I believe that it demonstrated its clinical value, but there eventuated a series of phenomena following the administration of the large dosage. First breast hypertrophy, then the first menses in nine years for a period of ten days, the further administration in larger dosage, 400,000 R.U. brought about intense hypertrophy of the breast and a second menses. There then followed an unusually long interval between attacks (seven weeks) during which the breast hypertrophy practically disappeared. This event causes us to consider the recent finding of Dean Lewis,<sup>11</sup> that in a fibroadenoma of the breast,

assay of the tissue for the female sex hormone showed it to contain much greater concentration per gram than the ovary. The question then arises, is the breast capable of storing the female sex hormone? From my experience in this case and in others I would answer in the affirmative. This is especially suggestive in the case of a male to whom the progynon B was given for a typical migraine with left-sided hemianopia. He developed pain in the nipples, and breast tissue appeared in the region of the left nipple following the administration of 30,000 R.U. of progynon B. In these two specific instances the attacks did not occur while the breast enlargement was evident.

Ingleby<sup>12</sup> in 1932 showed that both the normal breast and benign pathology of the breast undergo a sexual cycle, and we know that lack of ovarian stimulus causes atrophy to occur.

The concluding thought on this particular phase is that in cases of severe ovarian deficiency the therapy should be pushed until there are hyperplastic changes in the breast, because we know then that the blood content of the follicular hormone should be in the normal physiologic levels.

#### CONCLUSIONS AND SUMMARY

The benzonated female sex hormone (progynon B) when administered in sufficiently large dosage will produce menstrual bleeding in an amenorrhea of nine years' duration.

The administration of the benzonated female sex hormone combined with the anterior lobe extract, is effective in inducing menstruation in certain amenorrheas of one year's duration even when associated with progressive and extreme atrophic states of the ovaries and uterus such as is found in Simmond's disease.

The benzonated female sex hormone induced hypertrophic changes in hypoplastic uteri and breasts.

The benzonated female sex hormone is nontoxic in extremely high single and accumulative dosage.

The benzonated female sex hormone controls the melancholia associated with hypoovarian states and is also effective in migraine irrespective of sex.

#### REFERENCES

- (1) Allen, E., and Doisy, E. A.: *Am. J. Anat.* 34: 133, 1924.
- (2) Stockard, C. P., and Papanicolaou, G. N.: *Am. J. Anat.* 22: 225, 1917.
- (3) Butenandt, A.: *Naturwissenschaften* 17: 879, 1929.
- (4) Dodds, C., and Robertson, J. D.: *Lancet* 1: 1390, 1930.
- (5) Parkes, A. S.: *J. Anat.* 45: 275, 1931; *Lancet* 1: 188, 1932.
- (6) Schwenk, E., and Hildebrandt, F.: *Naturwissenschaften* 8: 177, 1933.
- (7) Zondek, B.: *Lancet* 2: 356, 1934.
- (8) Kauffman, C.: *Proc. Royal Soc. Med., Lancet* 1: 188, 1932.
- (9) Locser, A.: *J. Obst. & Gynec. Brit. Emp.* 41: 86, 1934.
- (10) Kauffman, C.: *Klin. Wchnschr.* 12: 217, 1933.
- (11) Lewis, D., and Geschickter, C. F.: *J. A. M. A.* 103: 1212, 1934.
- (12) Ingleby, H.: *Lancet* 2: 835, 1932.
- (13) Leyton, O.: *Lancet* 1: 1225, 1934.
- (14) Crile, G.: *Polyglandular Disease*. International Assembly Proceedings Unpublished.



## AN ANALYSIS OF 381 CESAREAN SECTION CASES IN A TEN-YEAR PERIOD AT MICHAEL REESE HOSPITAL\*

IRVING F. STEIN, M.D., AND MICHAEL L. LEVENTHAL, M.D.,  
CHICAGO, ILL.

IN VIEW of the existing enthusiasm over low cervical cesarean section, in 1927 the attitude of the obstetric staff of Michael Reese Hospital toward abdominal delivery changed abruptly. Prior to this period, cesarean section was performed in less than 1 per cent of our cases. After a two-year trial of the low cervical technic our indications were greatly broadened and consequently the operative incidence increased. We, therefore, have selected for analysis and study the two five-year periods just prior to and immediately following the change. The results of the first 40 low cervical operations performed by the authors were reported before this society in 1927.<sup>1</sup> In that series there were no maternal deaths. Encouraged by our results, and the satisfactory experience of other members of the obstetric staff, we felt justified in extending our indications, hence the material increase in incidence of cesarean section in the next five years. That this increase was justified will be shown in the comparative analysis which is embodied in this report. The mortality from the operation of cesarean section in our series was strikingly reduced by improvement in operative technic and in anesthesia. The operations herein reported were performed by eleven operators, most of whom were on the regular obstetric service at the hospital. Fully three-fourths of the operations were performed by the four obstetricians comprising the present attending staff. Three of these hold university professorial positions in the medical schools of Chicago (Rush), Northwestern, and Illinois.

### INCIDENCE

There were 381 cesarean operations of all types among 15,136 cases, an incidence of 2.52 per cent for the ten-year period, 1922-1932. In the first five-year period, the incidence of section was 0.91 per cent and in the second, 3.79 per cent. Approximately 20 per cent of the sixty-one cases in the first period were classical sections, while in the second period, the incidence of the latter dropped to 8 per cent, and transperitoneal cervical operations rose to 90 per cent of the 320 cases. There were but five Porro cesareans, all in the second period. Our general incidence of cesarean section is comparable to that of many of the larger obstetric services as reported in the literature. The Chicago Lying-In Hospital incidence for the years 1915-1929, as reported by Greenhill, was 2.06 per cent,<sup>2</sup> and that collected by E. v. Ammon<sup>3</sup> during approximately the same period, representing the contributions of thirty-five authors, ranged from 0.04 per cent to 17.27 per cent, with an average of 1.66 per cent.

\*Presented at a meeting of the Chicago Gynecological Society, February 15, 1935.

During the years 1926-1930 inclusive, the transverse incision (Kerr<sup>1</sup>) of the lower uterine segment was performed by us in eighty-four of the 271 low cervical operations. This technic was then discarded as we believed that it offered no special advantage over the longitudinal incision, and that it left a decidedly weaker scar in case of future pregnancy. While we encountered no actual ruptures in this group, several cases of a weak or thin scar were observed at the time of repeated cesarean section. The difficulty appears to be that the upper flap of the transversely incised segment retracts and becomes a thick edge which, when united to the thin lower edge, does not result in perfect approximation.

#### INDICATIONS

*Dystocia, contracted pelvis, and previous pathologic labor* appear as the leading indications in the ten-year period. The listing of indications into tables representing the two five-year periods makes obvious the fact that the increase in cesarean sections depended to a great extent upon the broadened indications in relation to *toxemia, repeated cesarean sections, sterilization, and organic heart disease.*

Test labor in most instances determined whether or not dystocia obtained, and the criteria of test labor varied more or less with the different operators. As we previously stated,<sup>1</sup> "What constitutes an adequate test of labor is a matter of dispute and must be decided after a careful study of each individual case." Our inclination at the present time is to limit rather than to extend the hours of trial labor. Forty-seven patients in this series were allowed to labor from twenty-five to sixty-seven hours before deciding upon abdominal delivery. We now believe this to be entirely too long a test. Many of these patients were also listed in the group of contracted pelvis. We no longer rely upon mensuration as the all-important criterion in determining the indication for section in contracted pelvis, but study the degree of disproportion by clinical and roentgenographic methods, and suitable instances, we permit a reasonable test of labor. We do not believe that the patient should be subjected to an ordeal resulting in utter exhaustion of the mother and jeopardy to the child in order to conform with a preconceived idea, that if given sufficient time, 75 per cent of women with moderately contracted pelvis will deliver from below.

In the group listed under *previous pathologic labor*, elective cesarean section was decided upon in such cases as *previous third-degree tear during a forceps failure and craniotomy*, and in cases of *repeated stillbirths*. In others, with a history of long labors with living children, test labor was permitted. The question of indications in cases of previous cesarean operations was also individualized. When one or more sections had been performed upon a patient, and sterilization was requested or advised, elective repeated section was performed. When the first section was performed for a complication which did not appear in the next labor, or was done after but a brief test labor, providing the convalescence from previous section was uneventful, test labor was allowed before deciding upon the repeated operation. *Sterilization* was secured chiefly by means of two methods, namely: cornual excision of the interstitial portion of the fallopian tubes, and by the Walthardt modification of the Madlener technic of tubal ligation.<sup>11</sup> In our series, sterilization was indicated in twelve patients with organic heart disease and was usually done with the advice of the medical consultant. In many of these patients, the cardiac condition coupled with the desirability of sterilization furnished a combined indication for abdominal delivery. In case of repeated cesarean operations, the desires of the patient and her husband were taken into account in arriving at a decision to sterilize. In all cases, both husband and wife were required to give written consent for the operation.

In regard to the indications for cesarean section in *abruptio placentae* and *placenta previa*, no explanation is needed except in the lateral and marginal types

of previa. When the cervix is uneffaced and not dilated in the primipara with placenta previa, cesarean section offers the quickest and safest method of delivery for both mother and child. At or near term, the low cervical technic is preferable. In the second five years in this series, five multiparas were operated upon for lateral or marginal placenta previa. One of these patients should definitely have been treated by other methods, a para x with nonviable twins. In the analysis of maternal deaths, this case furnishes a mortality.<sup>9</sup>

That a great increase in incidence of cesarean operations occurred in the group of women with *toxemia* is designated: there were four in sixty-one cases in the first five years, and fifty-seven in 320 cases in the second. There is no doubt in our minds that in nonconvulsive toxemia of the severe type which does not respond to controlled management, pregnancy should be terminated. Low cervical section under local anesthesia is the method of choice of the authors for primiparas in this group, and is extended to some multiparas in whom induction of labor is inadvisable. Fifty-two patients in this group were operated upon for nonconvulsive toxemia with no maternal and only two fetal deaths. Both of these babies were premature and died from atelectasis.

According to Stander,<sup>5</sup> 25 per cent of the 17,000 women who die in the United States as a result of childbirth each year, die of toxemia. Holland<sup>6</sup> reported a maternal mortality of 39.3 per cent in 231 cases of toxemia (including eclampsia), and a fetal mortality of 46.9 per cent. Gordon,<sup>7</sup> found a maternal mortality in Brooklyn of 16.2 per cent and a fetal mortality of 21.9 per cent in 210 cases of toxemia. In our series, there were sixty-one cases of both types operated upon with two maternal (3.28 per cent) and five fetal deaths (8.19 per cent), all prematures.

It is the policy of the obstetric staff of Michael Reese Hospital to select abdominal delivery for the noneconvulsive type of toxemia but not for eclampsia. However, there were nine patients with convulsive toxemia operated upon in the ten-year period with one maternal and three fetal deaths.

#### MATERNAL MORTALITY

In the decade, 1922-1932, in which 381 cesarean sections were performed, there were nine maternal deaths, a gross mortality of 2.36 per cent. Eight of these deaths are justly chargeable to the mode of delivery, while Case 2, in which an attempt was made, at the request of the husband, to obtain a living child from a woman moribund with pneumonia, is rightfully eliminated. By subtracting this one death, our corrected mortality is 2.10 per cent. This figure practically corresponds to our total mortality in low cervical cesarean section (2.08 per cent). This percentage of mortality compares favorably with v. Ammon's summary (thirty-five authors) in which there were 222 deaths in 5,365 transperitoneal sections with a gross mortality of 4.14 per cent and a corrected mortality of 2.14 per cent. The corrected mortality (v. Ammon) for classic section was 2.60 per cent and for the extra-peritoneal technic, 3.61 per cent.

According to Plass,<sup>8</sup> the general maternal mortality from cesarean section is 5 to 10 per cent, and in the above-mentioned compilation (v. Ammon), the general mortality in cesarean sections is 5.76 per cent and corrected, 2.67 per cent. Holland's average mortality in 1,954 operations (1910-1920) was 4.3 per cent.

#### FETAL MORTALITY

Three hundred and eighty-five babies were delivered by cesarean section, including four sets of twins, from 381 mothers. Two sets died, the first in a case of abruptio placentae, and the second were nonviable twins in a case of placenta previa. Of the two sets which survived, one was in a patient with eclampsia and the other in a

patient with organic heart disease. The total number of fetal deaths was nineteen, a gross mortality of 4.93 per cent; corrected, 2.33 per cent. The following ten cases were deducted in computing the corrected mortality:

1. 1922: Antenatal death—Transverse presentation, membranes ruptured; previous interposition operation.
2. 1922: Intrapartum death, dystocia; heart tones heard just prior to surgical preparation for section; stillborn full-term fetus.
3. 1927: Premature (six and one-half months) nephritic toxemia.
4. 1928: Stillbirth in patient moribund with pneumonia.
5. 1929: Premature (1,215 gm.) with atelectasis toxemia.
6. 1929: Premature (996 gm.) toxemia.
7. 1929: Premature (635 gm.) severe nephritic toxemia.
8. 1930: Anencephalic monster, previous cesarean section, sixteen-hour test labor.
- 9 and 10. 1931: Premature twins (six months), placenta previa.

The published fetal mortality in the period covered by this study varies somewhat. Thus, v. Ammon in his general summary, reported a 9.3 per cent gross and 3.95 per cent corrected fetal mortality in 7,287 births; Constantinesco, 18.7 per cent in classic and 6.3 per cent in low cervical section; Welz (1925), 11 per cent and Seeley (1930), 12.8 per cent, both from the city of Detroit; and Greenhill, 4.5 per cent from the Chicago Lying-In Hospital. Thus, the fetal mortality of 2.33 per cent in this series appears favorably low.

#### MATERNAL MORBIDITY

The morbidity in cesarean section is generally high, and in our series was 36.48 per cent. Eighteen different complications occurred in 139 patients, and uneventful recovery obtained in 242. The vast majority of complications occurred under the first five headings, conditions which, for the most part, did not threaten the life of the patient. The serious and even fatal complications such as sepsis, peritonitis, evisceration, and pulmonary embolus were but rarely encountered. The factors which we believe have an important bearing upon the chief morbid conditions observed in our series are as follows:

*Abdominal distention* occurred with much greater frequency when general anesthesia was used than with local, and most often with ethylene. There apparently was no relationship between distention and the state of the membranes, for in eighty-three cases, the membranes were ruptured for an average of fourteen hours before section was performed. Distention was noted in 19 per cent of the latter and in about 18 per cent of patients with intact membranes. Test labor likewise was of little significance, for in about 16 per cent of cases with labor (average, twenty-eight hours) and 20 per cent without labor, abdominal distention occurred. There was no difference in incidence of distention in patients after low cervical and classic cesarean section (18 per cent).

*Pyelitis* occurred two and one-half times as often with general as with local anesthesia, and most frequently with ether (15.9 per cent). It occurred twice as often after the membranes had ruptured for an average of twenty-three hours, and 59 per cent more frequently after test labor. It was decidedly more frequent after the low cervical operation for obvious reasons. First, the bladder is more or less completely detached from the lower uterine segment during the operation; and second, catheterization is more frequently done as a routine. The bladder is usually emptied every eight hours postoperatively, and frequently the catheterization is done on the same patient by two or three different student nurses.

*Wound infection* occurred approximately in the same percentage of patients with ether, ethylene and local anesthesia, but was slightly less frequent with local than

with ethylene; this is contrary to the general belief, that local infiltration favors wound infection. It was three times as frequent when the membranes were ruptured for an average of twenty-five hours as when they were intact, and twice as often in patients with an average test labor of twenty-five hours as in elective section. Probably the latter factors were also operative in the greater frequency of wound infection in low cervical as compared with classic cesarean section, for the latter was an elective operation as a rule.

*Sapremia* occurred twice as often after general as after local anesthesia, and most frequently after ether. In patients who were permitted labor (average, twenty-

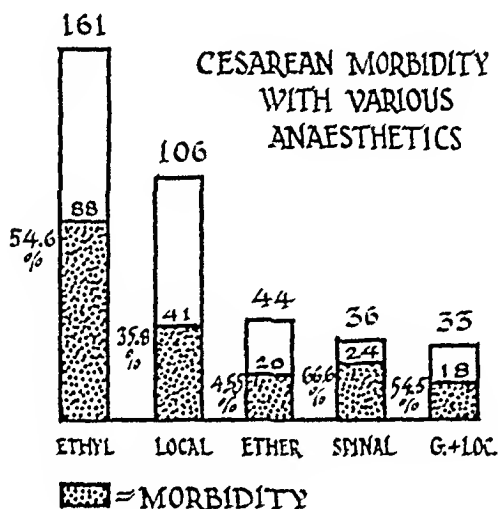


Fig. 1.—Morbidity chart.

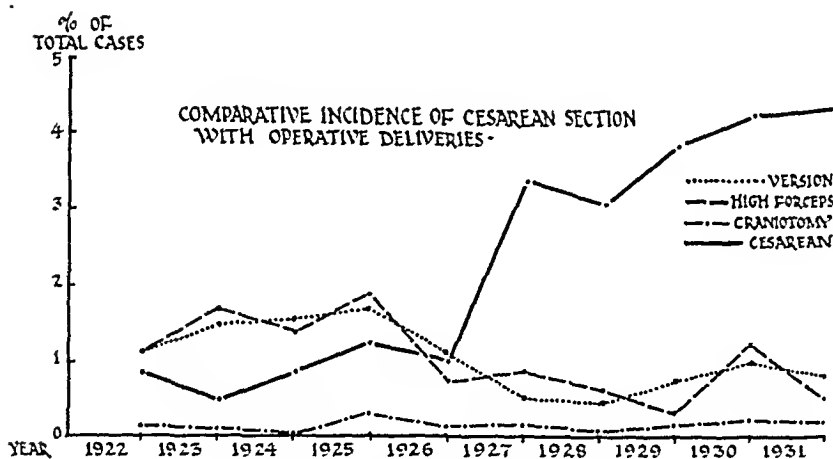


Fig. 2.—Comparative incidence.

seven hours), *sapremia* occurred twice as often as those operated upon before the onset of labor, and as with wound infection and pyelitis, a greater incidence of *sapremia* occurred after low cervical section.

*Respiratory infections* were entirely absent in the patients operated upon under local anesthesia and occurred with greatest frequency after ether anesthesia (6.28 per cent). They were more frequent, though few in number, in patients with ruptured membranes; in the patients with test labor they were less frequent. There were no respiratory infections in the 39 patients in whom classic cesarean was performed and but 3.23 per cent in the 337 patients with low cervical cesarean.

Fig. 1 illustrates graphically the general relationship of anesthesia to morbidity in our series. The lowest morbidity occurred with local infiltration and block, and the highest with spinal anesthesia. The addition of inhalation anesthesia to local anesthesia apparently increased the morbidity to the level of the general anesthesia group.

#### COMMENT

As will be observed from the accompanying graph (Fig. 2), when our cesarean incidence increased, there was a 50 per cent decrease in versions and high forceps operations. Craniotomies constituted a small but constant incidence throughout the decade. We are in full agreement with the conclusions of Baer, Reis and Lutz that the decrease of 50 per cent in the incidence of versions is not entirely justified, while that of high forceps is fully warranted. When we attempted to compare the morbidity from these three groups of operative deliveries, we encountered considerable difficulty in placing the correct evaluation upon significant factors. The conditions under which the operations are performed are frequently dissimilar, and the prerequisite conditions for one type of operation may entirely exclude the other. To obtain a proper perspective of the three competing operations, we have taken into account not only complications which we encountered, but have also included the gross maternal and fetal mortality. Thus, our gross maternal mortality from version during ten years was 3.24 per cent, high forceps, 0.67 per cent, and cesarean section, 2.36 per cent. The gross fetal mortality was 17.28 per cent in version, 8.13 per cent in high forceps, and 4.92 per cent in cesarean section.

That our choice of operative procedure in some instances might justly be criticized is realized as we look back over our results. In the group delivered by version and extraction, there were 42 primiparas and 11 patients in whom the membranes were ruptured for more than twelve hours. Among these, there were undoubtedly some who might more judiciously have been delivered by abdominal section. On the other hand, the patients with partial placenta previa and those with eclampsia who were delivered by section might have been delivered vaginally in strict accord with our policy, and with more favorable results.

It has been the policy of our staff to obtain a fetal roentgenogram before performing cesarean section to study the fetal development and pelvic disproportion, and also to detect fetal monstrosities and multiple pregnancy which may have gone unrecognized clinically. In many emergent conditions, however, the x-ray examination was omitted. Furthermore, due to economic conditions, many patients objected to the added cost of this type of examination as they believed it to be non-essential. In 73 patients (19 per cent) in our series, roentgenograms were obtained before abdominal section. Had routine roentgenograms been made, vaginal delivery might have been chosen in two cases of twins and unquestionably in the case of anencephaly referred to above.

## CONCLUSIONS

1. Cesarean section has taken an increasingly significant place among the operative procedures in the Michael Reese Hospital maternity.
2. The adoption of the low cervical technic is chiefly responsible for the extended indications and consequent increased incidence.
3. The maternal mortality from cesarean section in the ten-year period was 2.10 per cent and the fetal mortality was 2.33 per cent. These results compare favorably with the published statistics covering the same period.
4. Analysis and study of the postoperative complications yield some valuable information concerning the morbidity, but is of little assistance in determining a choice between vaginal and abdominal delivery.
5. The advantage of local over other forms of anesthesia is demonstrated by the analysis of morbidity. The highest morbidity occurred in the group operated upon under spinal anesthesia.
6. Comparative and combined maternal and fetal mortalities indicate that in our hands, cesarean section is safer than version and high forceps. We do not recommend the replacement of version by cesarean section, however, in cases that present valid indications and prerequisite conditions for the operation of version and extraction.

## REFERENCES

- (1) *Stein, I. F., and Leventhal, M. L.*: AM. J. OBST. & GYNEC. 16: 229, 1928.
- (2) *Greenhill, J. P.*: AM. J. OBST. & GYNEC. 19: 613, 1930. (3) *v. Ammon, E.*: Arch. f. Gynäk. 140: 66, 1930. (4) *Kerr, M.*: AM. J. OBST. & GYNEC. 12: 729, 1926. (5) *Stander, H. J.*: Toxemias of Pregnancy 15: 1929, Medicine Monographs, Williams & Wilkins Co., p. 70; Curtis' Obstetrics and Gynecology 2: Philadelphia, 1933, W. B. Saunders Co., p. 437. (6) *Holland, E.*: J. Obst. & Gynec. Brit. Emp. 28: 358, 1921. (7) *Gordon, C. A.*: AM. J. OBST. & GYNEC. 16: 307, 1928. (8) *Plass, E. D.*: AM. J. OBST. & GYNEC. 22: 126, 1931. (9) *Mussey, R. D., and Randall, L. M.*: Curtis' Obstetrics and Gynecology 1: Philadelphia, 1933, W. B. Saunders Co., p. 1037. (10) *Constantinesco, M.*: Ztschr. u. Ber. Gynäk. 13: 188, 1928. (11) *Reis, R. A.*: Curtis' Obstetrics and Gynecology 3: Philadelphia, 1933, W. B. Saunders Co., p. 232. (12) *Baer, J. L., Reis, R. A., and Lutz, J. J.*: AM. J. OBST. & GYNEC. 24: 599, 1932.

310 SOUTH MICHIGAN AVENUE

---

Brown, T. K., et al.: Pyridium in the Treatment of Gonorrhoeal Vaginitis in Children, J. Missouri M. A. 31: 313, 1934.

The authors report the results obtained in 21 children between the ages of two and ten years who have remained cured at least 6 months after cessation of treatment. The treatment consists of a vaginal suppository of 0.16 gm. of pyridium in boroglyceride of gelatin base inserted every night followed by a 500 c.c. of 1:1,500 KMnO<sub>4</sub> douche via Dakin tube under very low pressure every morning. Under such a regime the duration of treatment has been reduced gradually so that with a cooperative family the average treatment extends from four to eight weeks.

J. THORNWELL WITHERSPOON.

## PORRO CESAREAN SECTION\*

### AN ANALYSIS OF 53 CASES: SIGNIFICANCE OF INDICATIONS

A. F. LASH, PH.D., M.D., AND W. G. CUMMINGS, M.D., CHICAGO, ILL.  
(From the Obstetrical Department of the Cook County Hospital and the Department of Obstetrics and Gynecology, College of Medicine, University of Illinois)

**E**DOARDO PORRO of Pavia suggested amputation of the uterus following cesarean section in 1876 to overcome the high mortality (40 to 62 per cent). In the next twenty-five years the mortality dropped to 24.6 per cent, due to the decreasing incidence of infection following the introduction of antiseptics and asepsis. With further improvement in the technique of the cesarean operation, the Porro method has been employed only occasionally since it sacrifices the uterus. But though its field of usefulness has become narrowed it may be still the procedure of choice or necessity under certain conditions. The original technique has been modified so that only a supravaginal hysterectomy is performed, although the name is retained.

The indications recognized today are:<sup>5</sup> Intrapartum infection when vaginal delivery is not possible; fibroids, especially when they are obstructive; uterine hemorrhage which appears uncontrollable after a cesarean section for a premature separation of the normally situated placenta or placenta previa; rupture of the uterus; uncontrollable postpartum hemorrhage; placenta accreta; carcinoma of the cervix and osteomalacia. In addition to the above, we wish to emphasize the following indications, namely: combinations of above conditions, pulmonary tuberculosis, chronic nephritis, and sterilization.

The statistics of the fifty-three patients operated upon in the Obstetrical Department of the Cook County Hospital for the five-year period 1930 to 1934 are given in Tables I to V.

TABLE I

Race	{ White 26 Colored 27											
Age	{ 19-20 2 21-25 4 26-30 14 31-35 9 36-40 12 41-45 10 46-48 2											
Para	{ 0 1 3 6 ii 6 iii 3 iv 4 v 5 vi 7 vii 6 viii 6 ix 1 x 4 xi 1 xviii 1											

The Porro cesarean section performed in a multiparous woman past thirty-five years of age requires a single indication, but in a younger woman with one or no children the indication must be that of life

\*Presented before the Chicago Gynecological Society, February 15, 1935.



TABLE II. INDICATIONS FOR PORRO CESAREAN SECTION IN 53 PATIENTS

PRIMARY	ASSOCIATED PATHOLOGY OR ADDITIONAL INDICATION	TOTAL
Placenta previa centralis	Fibroids	2
	Preeclampsia, sterilization multiparity	1
	Multiparity	1
Premature separation of the normally situated placenta	With couvelaire uterus	8
	With intrapartum infection	2
	Multiparity, sterilization	2
Disproportion	Long labors, ruptured membranes	5
	Previous cesarean sections, sterilization	3
	Intrapartum infection	1
Preeclampsia	Intrapartum infection	3
	Sterilization, multiparity	3
	Feeble-mindedness	1
Chronic nephritis	Preeclampsia superimposed, sterilization	5
	Fibroids	1
	Placenta previa	1
Pulmonary tuberculosis	Sterilization	3
	Pott's disease, sterilization	2
Ruptured uterus		5
Threatened rupture of uterus	Ruptured membranes, 18 hours, multiparity	1
Neglected face presentation	Live baby; attempts at delivery at home	
	Membranes ruptured 24 hours; labor 60 hours	
	Intrapartum infection	1
Prolapsed uterus and vagina	No dilatation; strong labor pains 6 hours	
	48 years old, para ix	1
Sterilization for abnormal mentality		1

TABLE III. OPERATIVE PROCEDURES IN THE 53 PATIENTS

Classical cesarean section	15
Low cervical cesarean section	28
Subtotal hysterectomy	
After removal of child	46
Before removal of child	6
Complete hysterectomy	1
Salpingectomy	
Unilateral	3
Combined with oophorectomy	4
Bilateral	2

TABLE IV. MORBIDITY

Fever before operation	7	
Fever after operation		
100° F. and above after first postoperative day	37	69.8 per cent
Bag induction attempted	2	
Membranes ruptured 12 to 72 hours	10	
Labor present from 6 to 60 hours	20	
Wound infections	12	

TABLE V. MORTALITY IN THE 53 PATIENTS

Maternal	6	11.3 per cent
Fetal		
Before operation	19	35.8 per cent
After operation	3	5.7 per cent

preservation. The operation is not complicated, not time consuming and is usually followed by a smooth convalescence. Its greatest objection is that it sacrifices the uterus in the childbearing period and atrophy of the ovaries may follow five to eight years later. In our series the two women under twenty years of age, had, respectively, a ruptured and an infected uterus with a live baby in malposition. In the other young women combinations of conditions were present to demand the radical operation. Such combinations as placenta previa centralis and fibroids, chronic nephritis and fibroids require no detailed discussion as they are generally accepted.

Since tuberculosis is aggravated during menstruation and the puerperium, it was considered logical to eliminate these physiologic states by removing the uterus in those women in whom childbearing was contraindicated. Further, we utilized Petersen's work as a basis in attempting to decrease the capillary permeability by administering pituitrin in oil intramuscularly or intranasally for the first ten post-operative days. The reason for attempting to decrease the capillary permeability is to decrease the action of the proteolytic enzymes on the tuberculous lesions. These enzymes are in the blood during the puerperium and may break down the healing processes around the tubercle bacillus. All of the five tuberculous patients were operated under local anesthesia and all made smooth postoperative recoveries. There were only temporary rises in temperature in the first few post-operative days. All these women were sterilized on recommendation of medical consultants. Therefore, the function of the operation in tuberculous women is not only to sterilize when the condition warrants it, but also to eliminate the involution phenomena and future menstruation.

In chronic nephritis, we felt that by removing the uterus the load on the kidneys with lowered functional capacity was decreased. With involution there is an increase in nitrogenous end-products in the circulation due to the breaking down of the uterine musculature by autolytic processes. Slemons<sup>6</sup> showed that the characteristic increase in nitrogen output was lacking after a Porro cesarean section. In the experience of one of us (A. F. L.) a patient was observed to pass into a moderately severe uremia after delivery. Therefore, the value of a Porro cesarean section in chronic nephritis is not only as a sterilizing method in women with permanently impaired kidneys but also as a preventative for postpartum uremia.

In considering Porro cesarean section as a method for sterilization one must demonstrate the absence of increased risk over the other sterilization methods. Our series had no mortality in those cases in which sterilization was the only indication. Williams preferred this

method of sterilization to avoid future conception. Also the usual clinic patient is unable to return for a later sterilizing operation because of her household duties.

The high morbidity of 69.8 per cent can be expected in the light of Harris' histologic studies of amputated uteri from Porro cesarean sections. He found that in women with labors of six to eighteen hours' duration, 80 per cent of the uteri showed inflammatory reactions, and when the uterus was removed late in the first or second stage, 64.3 per cent showed such changes. From this information we should have expected a morbidity of 73.5 per cent because of the intrapartum infections, the duration of the rupture of the membranes, and long labors as shown in Table IV.

The mortality rate is high (11.3 per cent) and may be explained by the serious condition of the patients treated, since the operation is employed only as a last resort for delivery. There were some patients whose lives were saved by the operation. A striking example is that of a colored multipara with preeclampsia who had two bag inductions (extending over twenty-seven hours) which failed. She developed an intrapartum infection, and it was evident she could only be delivered from above. During the operation gas escaped from the vagina and the uterus was removed without opening it. Cultures from the uterus revealed *Bacilli welchii* and hemolytic streptococci. She recovered although she had a febrile postoperative course and an infected abdominal wound.

It is difficult to compare mortality statistics of various clinics because of the difference in indications and variation in conditions and types of patients. Thus Eardley Holland's series of 46 Porro cesarean sections showed a mortality rate of 17.4 per cent; Lazard in a series of 51 such operations reports 4 deaths or 7.8 per cent. Harris found in the 64 Porro operations done at the Johns Hopkins Hospital up to 1922, a mortality incidence of 4.68 per cent. Phaneuf reported 25 consecutive cases without maternal mortality.

Abstracts of the histories of the six maternal deaths are as follows:

CASE 1.—E. T., a colored, thirty-year-old para vi, with preeclampsia, had a bag induction which failed to induce labor but was followed by an intrapartum infection. A hysterectomy followed a classical cesarean section. The patient died of an acute fibrinous peritonitis on the eighth postoperative day.

CASE 2.—M. K., a white, forty-three-year-old para viii, with a preeclampsia superimposed on a chronic nephritis, having a blood pressure of 264/140 and a premature separation of the placenta, died from shock on the operating table.

CASE 3.—T. C., a colored, twenty-six-year-old para iv, had a disproportion with a two-hour labor and membranes ruptured ten hours. She showed evidence of an intrapartum infection, and a Porro cesarean section was done. She died of a generalized peritonitis on the tenth day.

CASE 4.—J. K., a white, twenty-one-year-old para ii, had a previous cesarean section and came to the hospital in labor. The occiput being below the spines she

was allowed to labor for twenty-six hours when she ruptured her uterus. At operation the baby was found in the peritoneal cavity. A septic course followed and she died from a diffuse suppurative peritonitis on the eleventh postoperative day.

CASE 5.—R. W., a white, forty-one-year-old para ix, had a placenta previa centralis. A classical cesarean operation was followed by a hysterectomy. She died of a generalized peritonitis on the sixth postoperative day.

CASE 6.—D. McK., a colored, thirty-seven-year-old para iii, a preeclamptic with a blood pressure of 250/190 and a placenta previa, had a low cervical cesarean section followed by a hysterectomy. The patient died of cardiac failure on the ninth postoperative day.

The brief details of the fatal cases indicate that infection is still a serious complication in spite of the radical procedure. Phaneuf advises drainage through the cervix even if it not absolutely necessary. His advice is certainly based on justifiable results, as mentioned above. The only patient of the whole series who had a drain through the abdominal wall was the one with the *Bacillus welchii* infection described above. It is evident that even the radical operation is hazardous in the presence of infection. Two of the deaths in Lazard's series followed infection. These two were from a group of nine cases of infections. Therefore, it may be advised from the experiences of others and ours, that in the presence of frank infection, every precaution should be taken to protect the peritoneal cavity from infection by eventrating the unopened uterus and carrying out all work extraabdominally and draining through the cervix.

#### SUMMARY

1. The Porro cesarean operation is not often performed but when necessary plays an important rôle in surgical obstetrics. The indications are usually life saving in infected or acutely anemic women, as during or following hemorrhage and, therefore, the mortality is high (11.3 per cent).

2. The indications being chronic nephritis, tuberculosis, or sterilization, the mortality should be much lower than when infection is present or nil.

3. Proper precautions and cervical drainage may be aids in preventing fatal peritoneal infections following Porro cesarean section.

#### REFERENCES

- (1) Harris, J. W.: Johns Hopkins Hosp. Bull. 33: 318, 1922. (2) Holland, E.: J. Obst. & Gynec. Brit. Emp. 28: 1921. (3) Lazard, E. M.: California & West. Med. 39: 156, 1933. (4) Peterson, W. F., and Lash, A. F.: Arch. Int. Med. 39: 12, 1927. (5) Phaneuf, L. E.: Am. J. Surg. 13: 65, 1931. (6) Slemons: Johns Hopkins Hosp. Bull. 21: 195, 1914. (7) Williams, J. W.: Obstetrics, ed. 6, New York, 1930, D. Appleton & Company, p. 549.

## CESAREAN SECTION\*

### AN ANALYSIS OF FIVE HUNDRED CONSECUTIVE OPERATIONS

EDWIN F. DAILY, M.D., CHICAGO, ILL.

#### INCIDENCE

*(From the Department of Obstetrics and Gynecology, University of Chicago)*

THE cases analyzed in this paper are the first 500 cesarean sections performed since the opening of the Chicago Lying-in Hospital in affiliation with the University of Chicago. There were 8,871 babies delivered in the hospital weighing 1,500 gm. or over, from May, 1931, to September, 1934. There were 8,622 white women delivered in their homes by home-delivery services. Their pathologic cases were sent to this hospital. The hospital does not admit negro patients.

The incidence of cesarean sections for the entire series (17,493) was 2.86 per cent.

The incidence of cesarean sections among the hospital cases (8,871) was 5.6 per cent.

There were 39 operators for the entire series, no one of whom operated upon more than 9 per cent of the 500 patients. The courtesy staff of the hospital, which consists of physicians in private practice, operated upon 24.8 per cent of the patients. Members of the Departmental Staff of the University of Chicago operated upon 75.2 per cent of the cases.

#### TYPES OF OPERATIONS

279 Laparotrachelotomies	55.8 per cent
182 Laparotrachelotomies and sterilization	36.4 per cent
30 Porro cesarean sections	6.0 per cent
8 Classical cesarean sections (4 sterilized)	1.6 per cent
1 Vaginal cesarean section	0.2 per cent
216 of the patients were sterilized	43.2 per cent
112 Madlener technic	51.8 per cent
74 Resection of tubes (Adair technic)	34.5 per cent
30 Porro sections	13.9 per cent

#### MATERNAL MORTALITY

The total maternal mortality for the 500 cesarean sections was 1.0 per cent. Of the five cases which died, two were operations performed antemortem to obtain a living child from patients with tubercular meningitis. One was a decompensated cardiac case, in critical condition at time of operation. One death resulted from

\*Presented at a meeting of the Chicago Gynecological Society, February 15, 1935.

postoperative intraabdominal hemorrhage from a bleeding omental vessel. The fifth death was the result of generalized infection in a patient with endocarditis of long duration.

#### MORBIDITY

The standard as advocated by the American Committee on Maternal Welfare was used in calculating the morbidity of these cases. Stander, in a recent article on morbidity and mortality, has used practically the same standard. Any patient with a temperature of 38° C. (100.4° F.) or over recorded on any two days after the first twenty-four hours postpartum, oral temperature readings being made at least four times daily, is regarded as febrile. All deaths are included in the morbidity figures whether there was a febrile morbidity or not.

Of the 500 cases 234 were febrile according to the above standard, or 46.8 per cent. (Average morbidity, British Standard, for all cases delivered in hospital, 15.4 per cent.) Twenty-three or 4.6 per cent of the patients remained in the hospital longer than fourteen days. Of the 279 patients having simple laparotomies 49.1 per cent became febrile. Of the 182 patients having laparotomies and sterilization 38.3 per cent became febrile. The lower morbidity in the sterilization group is explained by the fact that these operations were mostly elective. Of the 30 patients having Porro cesarean sections, 66.6 per cent became febrile. (Potentially infected cases.) Of the 8 patients having classical cesarean sections, 75.0 per cent became febrile. The one vaginal cesarean section was febrile.

*Influence of Labor on Morbidity.*—Of the 500 patients 162 or 32.4 per cent were in labor at time of operation; 59.9 per cent of the patients in labor at time of operation became febrile. Eighty-six patients were in labor twelve hours or more, 66.3 per cent of these became febrile. Seventy-six patients were in labor less than twelve hours, 52.6 per cent of these became febrile.

*Influence of Ruptured Membranes on Morbidity.*—Of the 500 patients 103 or 20.6 per cent had ruptured membranes at time of operation. Of the patients with ruptured membranes 62.2 per cent were febrile. Forty-two patients had ruptured membranes for over twelve hours; 69.0 per cent of these became febrile. Sixty-one patients had ruptured membranes for less than twelve hours; 58.3 per cent of these became febrile.

#### FETAL MORTALITY

There were 14 stillborn babies, eleven of whom were premature. Abruptio placentae accounted for 12 of these deaths, placenta previa for one, and eclampsia for one.

Seventeen babies, of which 14 were premature, died in the neonatal period. Abruptio placentae explained six of these deaths, placenta previa two, congenital heart two, eclampsia one, hydrocephalus one (lived two and one-half months), primary atelectasis two, and cause of death was undetermined in three. A total of 31, or 6.2 per cent of the babies were lost. Of these 25, or 5.2 per cent were premature. Abruptio placentae or placenta previa accounted for 4.2 per cent. (Average fetal mortality for all hospital deliveries of infants weighing 1,500 gm. or more, was 3.75 per cent.)

#### INDICATIONS FOR OPERATION

Many patients presented multiple indications for operation so that it was necessary to classify them according to the major factor in making the decision for operation in each case. Contracted pelvis, 200 cases, or 40.0 per cent; preeclampsia, 44 cases, or 8.8 per cent; placenta previa, 40 cases, or 8.0 per cent. Previous cesarean section (no other indication other than desire for sterilization or threatened

rupture of uterine scar of former operation), 39 cases, or 7.8 per cent; cardiac disease, 35 cases, or 7.0 per cent; abruptio placentae, 25 cases, or 5.0 per cent; dystocia dystrophy syndrome, 22 cases, or 4.4 per cent; chronic nephritis, 20 cases, or 4.0 per cent; cervical dystocia, 12 cases, or 2.4 per cent; cephalopelvic disproportion, 10 cases, or 2.0 per cent; eclampsia, 8 cases, or 1.6 per cent; previous repeated stillbirths, 8 cases, or 1.6 per cent; fibromyomas of uterus, 5 cases, or 1.0 per cent; elderly primipara, 4 cases, or 0.8 per cent; umbilical or ventral hernia, 4 cases, or 0.8 per cent; diabetes mellitus, 3 cases, or 0.8 per cent; prolonged labor with uterine inertia 2, previous Dehrssen's incisions and difficult delivery 2, Bandl's ring 2, pulmonary tuberculosis 2, tuberculous meningitis 2, tuberculous hip 1. Carcinoma of the cervix, hydronephrosis, transverse presentation, Gaucher's disease, brain tumor, purpura hemorrhagica, twisted ovarian cyst, and acute cholecystitis, one each.

### PREVIOUS CESAREAN SECTIONS

Of the patients in this series 144 or 28.8 per cent had a previous cesarean section; 115 or 23.0 per cent had one previous cesarean section; 27 or 5.0 per cent had two previous cesarean sections; 2 or 0.4 per cent had three previous cesarean sections.

The majority of the previous cesarean sections had been performed in other hospitals, many were classical, and in a few there was definite defect in the uterine scar. We do not adhere to the dictum "once a cesarean always a cesarean." Of the 144 patients with a previous cesarean section 104 or 72.2 per cent were sterilized; 80 or 69.0 per cent of the 115 patients with one previous cesarean section were sterilized; 23 or 85.2 per cent of the 27 patients with two previous cesarean sections were sterilized; 2 or 100 per cent of the 2 patients with three previous cesarean sections were sterilized.

A patient is not sterilized with her first cesarean section unless she is suffering from an organic disease which future pregnancies would aggravate. If a second cesarean is indicated and the patient and her husband request sterilization, it is performed. We advise that the patient be sterilized at the time of a third cesarean section.

### PREVIOUS STILLBIRTHS

Of the women who had previously borne children 22.4 per cent had had stillbirths; 43.2 per cent of the multiparas who had no previous cesarean section had had stillbirths; 45 had one previous stillbirth; 19 had two previous stillbirths; 2 had three previous stillbirths; 1 had four previous stillbirths.

The majority of the previous stillbirths resulted from prolonged labors, difficult instrumental deliveries and neglected cases. The indication for cesarean section in most of the cases was contracted pelvis, but in a few cases cesarean sections were done because of the history of previous difficult deliveries and resultant stillbirths.

### PERIOD OF GESTATION

Ten per cent were from forty-one to forty-four weeks, 48.8 per cent were in the fortieth week, 34.4 per cent varied from thirty-six to thirty-nine weeks, and 6.8 per cent were from twenty-seven to thirty-five weeks.

The operations performed before the thirty-sixth week of gestation were almost entirely upon patients having abruptio placentae or severe toxemia as indications. Although the fetal mortality is high in the group under thirty-six weeks' gestation, it would have been higher with delivery from below using bags or other methods of mechanical induction, etc. We feel that the maternal risk in an abruptio placentae of any degree of severity is less when treated by cesarean section.

## ANESTHESIA

Our anesthetic of choice for laparotrachelotomy is novocaine, one-half per cent used for local infiltration. Medication with morphine and scopolamine may be used as the operation is started, because we believe there is little effect on the fetus if it is delivered within one hour. More sedative may be given if necessary after the baby is born. There were no fetal deaths in this series attributed to morphinism.

Ethylene is used to supplement local anesthesia when necessary. Some patients in labor are difficult to control under local anesthesia and ethylene is the initial anesthetic. Ether is added only when ethylene fails to relax the patient sufficiently.

Recently a few patients have been operated upon under avertin and local anesthesia when local alone was not thought suitable. Too few of these cases have been observed to draw any conclusions. Local anesthesia alone, 324 cases, 64.8 per cent; local and ethylene 65 cases, 13.0 per cent; local, ethylene, and ether 8 cases, 1.6 per cent; ethylene 65 cases, 13.0 per cent; ethylene and ether 32 cases, 6.4 per cent; ether 1 case, 0.2 per cent; avertin and local 5 cases, 1.0 per cent.

## FATAL CASES

1. Mrs. L. G., aged twenty-four, grav. i, para i (No. 88306). Admitted Aug. 16, 1933 when thirty-three weeks pregnant. In coma for five days, critical condition. Spinal fluid pressure 6.00 mm. H<sub>2</sub>O, yellowish, Ross Jones one-plus, 27 drops reduced 5 c.c. Benedicts, cell count 236 chiefly lymphocytes. Neurologic diagnosis: tuberculous meningitis.

Aug. 18, 1933: At request of family an autemortem classical cesarean section was done, delivering a 2560 gm. baby that is now living and well. Patient died four hours postoperative. No autopsy.

2. Mrs. E. A., aged twenty-two, grav. i, para i (No. 60403). Admitted July 18, 1932 when thirty-seven weeks pregnant. Sputum positive for tubercle bacilli. X-rays showed far-advanced bilateral pulmonary tuberculosis. Temperature for eight days preoperative averaged 101° F. and pulse 115. Condition critical with rapidly developing symptoms of meningeal involvement. Patient irrational.

July 26, 1932: Low cervical cesarean section under a local anesthetic. Baby weighed 2,795 gm. and survived. Patient became progressively worse. Inoculations of spinal fluid into guinea pig; tubercle bacilli recovered.

Died Aug. 6, 1932. Autopsy report: Generalized miliary tuberculosis with tuberculous meningitis.

3. Mrs. M. C., aged thirty-six, para vi, grav. vii (No. 48831). Admitted Jan. 30, 1932 when thirty-two weeks pregnant complaining of shortness of breath, chronic cough, edema of extremities, extreme weakness. Blood pressure 184/112. Pulse 100 to 110, blowing systolic murmur. R.B.C. 2,880,000. Hb 50 per cent. Diagnosis: Acute cardiac decompensation with mitral lesions, secondary anemia, chronic nephritis. Intravenous digitalis therapy for six days. Feb. 4, 1932: 500 c.c. blood transfusion. Feb. 5, 1932: Low classical cesarean section with tubal ligation under local anesthesia. Heart began fibrillating two hours later. Died of acute cardiac failure seventeen hours postoperative. Pathologist's report: chronic rheumatic mitral endocarditis with mitral stenosis and recent organizing subacute vegetative endocarditis. Generalized hypertrophy of the heart, chronic passive congestion of the lungs. Baby weighed 2,180 gm., died at age of two and one-half months of bronchial pneumonia.

4. Mrs. J. S., aged twenty-three, grav. ii, para ii (No. 44123). Admitted Jan. 13, 1932 when thirty-three weeks pregnant. Previous delivery three years ago else-



where by cesarean section after attempted forceps, vesicovaginal fistula followed. Generally contracted pelvis. Chills and fever with backache for two days before admission. Urine loaded with pus.

Diagnosis: Pyelitis complicating pregnancy. Temperature fluctuating between 102 and 104° F. for two weeks before infection subsided. Second two weeks of hospitalization temperature averaged 99°, probably due to chronic urinary infection resulting from fistula.

Feb. 13, 1932: Low cervical cesarean section under a local anesthetic. Uterus and omentum adherent to anterior abdominal wall, many adhesions ligated and incised. Patient went into shock twenty hours postoperative. Intravenous glucose and acacia solutions given while donors were coming in. Twenty-five hours postoperative diagnosis of intraabdominal hemorrhage was made, laparotomy done and omental bleeders tied. Patient died on operating table. Diagnosis: Exsanguination anemia from small omental vessels.

5. Mrs. I. G., aged twenty-five, grav. ii, para i (No. 97506). Admitted May 29, 1934 when thirty-nine weeks pregnant with dyspnea on exertion, palpitation and edema of extremities. Rheumatic heart disease had been diagnosed early in pregnancy. Medical diagnosis on admission: mitral stenosis and further pregnancies were felt to be contraindicated.

June 1, 1934: Low cervical cesarean section and tubal ligation under local, avertin and ethylene anesthesia. Patient had been in labor two hours. Prolonged septic postoperative course with peritonitis. Oxygen tent used night and day for several weeks. Numerous blood transfusions and other supportive therapy.

July 27, 1934: Attempt to drain perisplenic abscess failed. Allowed to go home Aug. 14, 1934 at request of family although condition was very poor. Temperature had been averaging 99° for four days previously. Died at home Aug. 18, 1934. Autopsy diagnosis: Mitral stenosis with recent vegetative endocarditis, multiple infarcts of lungs and spleen, pelvic thrombosis, endometritis, parametritis, subacute peritonitis with multiple adhesions and abscess formation.

---

Ludwig, Fritz: Operative Treatment of Congenital Umbilical Hernia, *Ztschr. f. Geburtsh. u. Gynäk.* 105: 308, 1933.

Congenital umbilical hernia occurs about once in 6,600 deliveries. The prognosis is always grave. Hernias vary in size from small protrusions to complete evagination. In German literature 125 cases are reported during the last fifty years; 86 of these were operated and cured. Most cases are not reported because the infants died either from operation or from conservative measures. The writer has operated upon three infants within a few hours after delivery. One baby died, two were cured, one of which required a second operation because of intestinal obstruction many years later. Operation very soon after a delivery, performed with utmost sterile technic, affords the most favorable chances; delay means infection.

GROVER LIESE.

## A REVIEW OF TWENTY-SIX CASES OF EXTRAPERITONEAL (LATZKO) CESAREAN SECTION\*

JAMES F. NORTON, A.M., M.D., F.A.C.S., JERSEY CITY, N. J.

*(From the Margaret Hague Maternity Hospital)*

**F**REQUENTLY enough, one encounters on a general obstetric service, patients long in labor, with a live baby, presenting part unengaged, or only fixed at the inlet, membranes ruptured, having had many vaginal and rectal examinations, perhaps with attempts at delivery vaginally, and either frankly or potentially infected, and in whom delivery from below with satisfactory results for both mother and child are not to be expected. Termination of such a labor vaginally can be accomplished only by undertaking procedures which, from the standpoint of the fetus, will yield either a severely traumatized infant or one with absolutely no chance of survival.

So far as the mother is concerned, if one could proceed in the presence of the above facts, and effect delivery by means of a cesarean section, and have no dread of subsequent sepsis, the solution would be easy. One would then have no further concern with the many disagreeable features and attendant technical difficulties of the alternative choice of a vaginal procedure; and the almost certain extensive traumatization of the maternal soft parts and the depressing shock associated with termination by the vaginal route would be circumvented. But in the type of case before indicated, can one proceed to use a transperitoneal approach to the uterus and feel reasonably sure that his efforts will not be thwarted by a subsequent fatal peritonitis?

Any study of the various statistical surveys shows clearly that, while the operation known as laparotrachelotomy or double flap, or a low cervical type of section is unquestionably far safer, and should, in the very great majority of all cases, supplant the old high classical type of operation, yet the same figures, just as unerringly, indicate that any transperitoneal operation in frankly infected or potentially infected cases which have been long in labor does not yield uniformly satisfactory results for the mother. Even with the far wider use of the lower segment type of operation, the problem of peritoneal infection following upon cesarean section still remains a formidable factor in all classes of cases, and infinitely more so in the so-called frankly infected or potentially infected group.

---

\*Read before the Section of Obstetrics and Gynecology, New York Academy of Medicine, January 22, 1935.

One feels that if the field could be approached abdominally, and the peritoneal cavity spared invasion, this would offer our best method of procedure. It is generally conceded that the best results can be obtained, as far as protecting the peritoneum is concerned, by making use of a true extraperitoneal approach to the lower segment.

We present here a small series of 26 cases in which we have utilized the extraperitoneal type of operation following the technic ascribed to Latzko and popularized in New York by Jellinghaus. We are not offering this series with the idea of presenting any new facts concerning this operation, neither do we wish to go into any exhaustive theoretical presentation concerning its advantages. We are concerned with only the presentation of the observations and facts gleaned from our own experience with the operation. I will not discuss here in any further detail the indications for, nor the advantages of, the operation. Neither will I set forth the technic, for all this follows closely that described previously by Steele<sup>1</sup> and Burns.<sup>2</sup> The disadvantages cited by

## RECORD OF CASES

TABLE I

NUMBER OF CASES	AGE	PARITY	HOURS IN LABOR WITH RUPTURED MEMBRANES		TOTAL HOURS IN LABOR	
26	Youngest 19.0	P. 20	Shortest	15.0 (2)	Shortest	9.5
	Average 26.5		Average	36.5	Average	41.0
	Oldest 38.0	M. 6	Longest	90.5	Longest	94.5

Of the 26 cases, 6 occurred in multigravidas. Of these 6 cases, 2 had only abortions, and no labors at term. Of the remaining 4 cases, one was a para vi, gravida vii, with membranes ruptured thirty-eight hours and in active labor forty-three hours. She was admitted to the hospital after an attempt at delivery with forceps in her home under ether anesthesia. Blood pressure 190/110, preeclampsia. The fetal heart was heard immediately before operation. A stillborn fetus was delivered by Latzko section.

A second case, para ii, gravida iii, in active labor for forty-eight hours with ruptured membranes for an uncertain length of time. Her first labor, complicated by eclampsia and terminated by forceps, resulted in a stillbirth. Her second labor was induced by bag insertion, and resulted in another stillbirth. In her third labor, a normal living baby was obtained by section.

The third case was a para i, gravida ii. First labor 16 months previous, terminated by forceps. There were extensive perineal lacerations, with repair; was in bed for 6 weeks following her repair. This labor began with ruptured membranes; she was in labor for twenty-one hours, with membranes ruptured for the same period of time. Live baby.

Fourth case, para ii, gravida iv, had one abortion. Her first labor was terminated with forceps at term, stillbirth; second labor, forceps with neonatal death in twenty-four hours. This labor began with ruptured membranes, and after forty-one hours, section performed and live baby obtained.

Table I, showing the average length of time with ruptured membranes as 36.5 hours, and the average length of labor as 41 hours, indicates that the operation was not undertaken in this series until it became very evident that, with a long trial of labor, no progress could be hoped for.

Of the 26 cases, 16 had ruptured membranes longer than the average period of time (36.5 hours); 14 cases had an active labor longer than the average length of time (41.0 hours).

The case in labor 9.5 hours had ruptured membranes for over twenty hours.

TABLE II

NUMBER OF CASES	TYPE OF PELVIS	ENGAGEMENT	NUMBER OF VAGINAL EXAMINATIONS	NUMBER OF RECTAL EXAMINATIONS
26	Normal 1	Yes 0	0-3	1-22
	Abnormal 25	No 26		

There was but one normal pelvis in the entire group (case of placenta previa, previously bagged), who developed an intrapartum temperature of 103.8° F. In all cases there is noted either a definite "flat pelvis," or "generally contracted," or "generally contracted flat" pelvis or a "cephalopelvic disproportion." In no case was engagement of the presenting part present before operation.

TABLE III

*Preoperative Morbidity and Complications:*

- 8 cases had temperatures from 99° to 100.3°
- 5 cases had temperatures from 100.4° to 103.8°
- 1 attempt with forceps and ether outside of hospital
- 3 cases were bagged
- 1 placenta previa
- 2 cases had medical induction
- 1 adenoma of thyroid
- 4 preeclampsia toxemia

13 of the 26 cases had a preoperative or intrapartum rise of temperature. Five cases had temperatures from 100.4° to 103.8° F.

While the other preoperative complications are listed in this table, they in no way figured in the indication for the operation, except the one case of attempted forceps outside the hospital.

The case with placenta previa was a marginal type of implantation, bagged, which had a temperature rise to 103.8°; in labor twenty-nine hours with membranes ruptured twenty-eight hours.

TABLE IV

TOTAL NUMBER OF CASES	ANESTHESIA	NUMBER OF OPERATORS	PERITONEAL CAVITY OPENED	BLADDER INJURED	AVERAGE TIME FOR OPERATION
26	Spinal 23	4	Yes 9	Yes 2	55-60 min.
	Spinal and Ether 2		No 17	No 24	
	NO <sub>2</sub> and Ether 1				

The spinal anesthesia used in the 23 cases was 100 mg. of novocaine crystals. In the two cases where ether was added to the spinal anesthetic, the time consumed from the administration of the anesthetic to the completion of the operation was too great to expect continued effectiveness from the spinal anesthesia.

The peritoneal cavity was inadvertently opened in 9 cases; these will be discussed in detail in the subsequent table.

The bladder was injured in 2 cases. In one case the opening was repaired at the time of operation by purse-string suture. The other case, on the second postoperative day, developed a urinary fistula through the abdominal incision, which healed spontaneously on the twelfth postoperative day.

The fifty-five to sixty minutes required for the performance of the operation are not considered unduly long when it is remembered that these are the first cases of this type coming out of our institution.

practically all commentators, and summarized by Burns, are: (1) Possibility of opening the peritoneum, and thus defeating the purpose of the operation. (2) Danger of injury to either the ureter or bladder. (3) Difficulty of performance and the length of time consumed.

TABLE V  
PERITONEAL CAVITY OPENED 9 CASES

MEMBRANES RUPTURED HOURS	ACTIVE LABOR	HIGHEST POSTOPERATIVE		
		TEMPERATURE	PULSE	RESPIRATION
35.5	47.0	99.2	96	26
90.5	45.0	99.6	92	18
28.0	72.0 (approx.)	100.4	114	16
25.0	24.0	100.4	96	22
70.0	94.0	101.2	92	26
60.0	62.5	101.0	100	22
72.0	21.0	99.6	112	22
38.0	41.5	99.4	104	20
17.0	34.0	100.4	100	24

Table V shows in somewhat greater detail the postoperative course of the 9 cases where the peritoneal cavity was inadvertently opened. In all cases search was instituted for any rent in the peritoneum before the uterine incision was made. If one was discovered it was repaired before the uterus was incised. In some few cases, however, a hole was made into the peritoneal cavity during extraction of the head. This was repaired immediately. It is interesting to note in connection with these 9 cases, where the membranes had been ruptured for an average of about forty-eight hours, and active labor had gone on for about forty-nine hours, and the peritoneal cavity inadvertently entered, that the highest postoperative temperature was 101.4°.

TABLE VI  
POSTOPERATIVE COMPLICATIONS

1 Cystitis and thrombophlebitis
1 Pyelitis
1 Vesical incontinence (cured)
1 Vesicoabdominal fistula (healed)
1 Pneumonia (spinal)

The only troublesome postoperative complications were (1) the vesical incontinence, which occurred in a case in which a retention catheter was needlessly employed for a long time, causing an edema of the bladder neck, and (2) the vesicoabdominal fistula which healed spontaneously.

The case of pneumonia was the placenta previa marginalis, bagged, with intrapartum temperature of 103.8°, which was later thought to be the first indication of the onset of the subsequent pulmonary complication. Spinal anesthesia was used in this case, but was not considered to be contributory.

TABLE VII  
INFANT MORBIDITY AND MORTALITY

NUMBER OF CASES	DISCHARGED IN GOOD CONDITION	STILL- BIRTHS	NEO- NATAL DEATH	TOTAL OBSTETRICAL MORTALITY	CAUSES OF DEATH
26	22	3	1	4	(3) Intrauterine asphyxia

The three stillbirths were ascribed to intrauterine asphyxia and were considered to be due to the length of labor and the poor condition of the fetus at the time operation was undertaken. In all, the fetal heart was heard immediately before the operation was undertaken.

The neonatal death occurred on the second day postoperative from atelectasis.

I will attempt to demonstrate that, in this small series, we obtained what we consider better results from both maternal and fetal stand-points than we would have dared hope for with any other method of procedure, and that the objections above cited do not seem valid.

May I add here that the observations and conclusions included in this paper represent not alone the thoughts of the author but rather the consensus of all the operators from whose services the cases embodied in this report are taken.

TABLE VIII  
MATERNAL MORBIDITY AND MORTALITY

NUMBER OF CASES	NO. OF CASES MORBID	AVERAGE NUMBER OF DAYS MORBID	DAYS IN HOSPITAL POSTOPERATIVE	DEATHS
26	18	4 days	Shortest 12 (2) Average 19 Longest 33	None
		15 longest		

Of the 26 cases operated upon, 15 had a marked postoperative course. The standard of morbidity used was a rise in temperature to 100.4° F. on any 2 readings following the first twenty-four hours on patients having their rectal temperatures recorded every four hours.

Four days was the average length of the morbid course in these 15 cases.

The longest postoperative stay was thirty-three days, in the case with the urinary incontinence.

There were no maternal deaths.

#### CONCLUSIONS

1. Obstetric problems may present themselves which can be adequately handled only by an abdominal type of delivery.

2. Infection of the peritoneal cavity, which is the chief deterrent in the utilization of the abdominal route, may be avoided, and a satisfactory maternal and fetal outcome anticipated, in a very high percentage of cases by a true extraperitoneal approach to the lower uterine segment.

3. The objections to this type of operation; namely, (a) invasion of the peritoneum, (b) bladder injury, (c) length of time consumed in the performance, should not be considered insurmountable difficulties for the obstetric surgeon.

4. Our experience with the inadvertent opening of the peritoneal cavity seems not to justify the statement that it defeats the purpose of the entire operation.

5. With the Latzko type of operation at his command, the obstetric surgeon may still perform the cesarean section with safety for both mother and child in many cases otherwise beyond his reach.

Grateful acknowledgment is hereby made to Drs. S. A. Cosgrove and P. O. Hall, and the late Dr. J. A. Binder, for permission to use the cases from their services.

#### REFERENCES

- (1) Steele, K. B.: AM. J. OBST. & GYNEC. 19: 747, 1936. (2) Barns, H. T.: AM. J. OBST. & GYNEC. 19: 759, 1936.

# THE THERAPEUTIC VALUE OF LOW-DOSAGE IRRADIATION OF THE PITUITARY GLAND AND OVARIES IN FUNCTIONAL MENSTRUAL DISORDERS\*

CHARLES MAZER, M.D., AND LOUIS SPITZ, JR., M.D., PHILADELPHIA, PA.  
(From the Department of Gynecology, Mount Sinai Hospital)

IN THIS purely clinical presentation of the subject, we studiously avoid discussion of the controversial problem of the mechanism whereby small doses of roentgen rays enhance functional activity of the ovaries or any other gland of internal secretion. We wish, however, to clarify our conception of the term "x-ray stimulation" very often employed synonymously with the term "low-dosage irradiation." They connote an increase in cell activity without evident microscopic changes in structure, produced by a dose only slightly greater than the one employed in extensive diagnostic procedures, nevertheless sufficient to excite changes in the equilibrium of the cell constituents. That the secreting elements of glands may hyperfunction or underfunction without evident alterations in cell structure is strikingly illustrated by the absence of histologic changes in the islands of Langerhans in some cases of hyperinsulinism and in nearly half of the diabetics who come to autopsy. It, therefore, is apparent that biochemical factors alone, such as cell permeability and arrangement of electrons, atoms, and molecules, often determine the degree of cell activity.

The phenomenon of cell stimulation should not be confused, however, with that of cell irritation. The latter, according to Lehmann,<sup>1</sup> is the summation of oft-repeated stimulation and eventually leads to destruction of the cell. "True stimulation," he states, "is present when after a small dose of rays or a small number of repetitions there occur phenomena of functional stimulation not followed by inverse effects in the irradiated gland." Restoration of ovarian function and of menstrual periodicity through low-dosage irradiation of the pelvis, therefore, is evidence of true stimulation in contradistinction to the improvement in genital function that occasionally follows destructive irradiation of pituitary or adrenocortical adenomas. X-ray effects short of cell injury are not demonstrable by the instruments at our disposal. They manifest themselves in the form of accelerated function.

## SELECTION AND CLASSIFICATION OF THE CLINICAL MATERIAL

In this study we merely present the summation of our observations on the effects of a given dose of roentgen rays on the menstrual cycles of

\*Read at a meeting of the Obstetrical Society of Philadelphia, March 7, 1935.

normal, amenorrheic and metrorrhagic women, followed up for periods averaging over two years. The patients were carefully examined to exclude factors not directly related to pituitary and primary ovarian deficiencies as the responsible agents for the menstrual disturbances. The possible presence of an early pregnancy was eliminated by physical examination and, when necessary, by means of the standard biologic tests. Cured or improved patients who received simultaneously, with or soon after x-ray treatment, some form of organotherapy are excluded from this study on the assumption that the latter may have contributed to the good results. Patients who failed to respond to combined roentgen ray and endocrine therapy are, on the other hand, included in our list of failures because of our conviction that the endocrine products were not responsible for the lack of response to the irradiation. We have also excluded from our statistical study those patients whose follow-up period is less than a year and, from our list of cures, those who failed to respond within two months after termination of treatment. Adherence to these rigid requirements, set up as a guard against erroneous deductions, justifies the presentation of this report because the literature on the subject lacks these elements of security against too hasty and unfounded conclusions.

Of the 102 patients comprising the study, 51 had pronounced amenorrhea; 21 had menstrual periods (with or without prolonged or excessive flows) at intervals of six to thirteen weeks; 13 were definitely metrorrhagic in type; 6 had excessive flows at normal intervals; 5 had short and scanty flows at normal intervals; and the remaining 6 were menstruating normally but were sterile for no accountable reason.

#### DOSAGE AND TECHNIC

The treatment of the patients was entrusted to three roentgenologists who, by agreement, employed a uniform dose and technic. The patients received three weekly exposures of the pituitary gland and ovaries. The technic employed is described by one of them (Edeiken<sup>2</sup>) as follows: "In the patient of average size, the technical factors are 127 K.V., 5 M.A., 14 inch distance, 5 M.M. aluminum filter for 3 to 5 minutes. This is equivalent to  $7\frac{1}{2}$  to  $12\frac{1}{2}$  per cent S.E.D. or 50-80 R. This dosage is varied according to the size of the abdomen and the thickness of the abdominal wall. . . . The central ray [in the pituitary exposure] enters just above and posterior to the midpoint of a line drawn between the outer canthus and the external auditory canal." In nearly half of our patients, the pituitary gland and the ovaries were treated simultaneously; in the others, the exposures were made alternately at three- to four-day intervals. The results are approximately the same in both groups of patients.

Five of the fifty-one amenorrheic patients with definite evidence of adiposogenital dystrophy received pituitary irradiation alone; three were cured; and two failed to respond. Four patients suffering from the amenorrhea of primary hypogonadism were treated by irradiation of the ovaries alone; two were cured and the condition of the other two remained unchanged. Unless it is certain that the menstrual disturbance is due to a primary hypogonadism, the pituitary body as well as the ovaries



should be treated. Irradiation of the pituitary gland alone, even in frank cases of adiposogenital dystrophy, will probably prove to be less effective in a larger group of patients.

#### SAFETY OF LOW-DOSAGE IRRADIATION OF THE OVARIES

No roentgenologist fears low-dosage irradiation of the pituitary gland, since experience with intensive treatment of pituitary adenomas has shown how resistant the normal elements of the gland are to x-rays. The profession, as a whole, and roentgenologists, in particular, are reluctant, however, to expose the ovaries even to mild irradiation because of the reports of Frank<sup>3</sup> and others that the temporary amenorrhea of some patients had become permanent as a result of such treatment. In mentioning these untoward effects, the authors unfortunately fail to state the respective age of the patients and the doses employed—factors of great importance. It is possible, moreover, that these partly amenorrheic women would have lapsed into a state of permanent amenorrhea without the use of x-ray treatment. It is evident, therefore, that possible harmful effects can be determined more accurately through studies of the menstrual rhythm of regularly menstruating women subjected to ovarian irradiation of similar dosage.

For this purpose we have carefully recorded for a period of nearly three years after low-dosage irradiation of the ovaries and pituitary gland the menstrual cycles of eleven regularly menstruating women, six of whom were sterile without apparent cause and five of whom complained of hypomenorrhea. *In none of them was the menstrual rhythm affected by irradiation in doses within the limits indicated above.* This, in our opinion, is sufficient clinical proof of the safety of the procedure and discounts definitely the impression of harm when occasionally a partially amenorrheic woman incidentally passes into a more permanent state of amenorrhea following low-dosage irradiation of the ovaries. We have encountered this sequence of events in only two of sixty-nine partially amenorrheic women thus treated. We must, nevertheless, remember that the margin between the safe and harmful dose is probably limited. Variation in dosage should, for the present, not exceed that employed in the treatment of our patients. Further evidence of the harmlessness of the procedure is the fact that seven of eleven of our amenorrheic patients, who had received more than one course of x-ray exposures at intervals of three months, were restored to normal menstrual periodicity, and that in none of the remaining four was the condition thereby aggravated.

One of the six regularly menstruating but functionally sterile women subjected to irradiation bore two healthy children. Another one is near term of pregnancy. The hypomenorrhea of the five in the group of eleven was not improved by the treatment, confirming our impres-

sion that the cause of hypomenorrhea lies in the lack of responsiveness of the uterine mucosa and that the condition is independent of the pituitary-ovarian mechanism.

In the category of regularly menstruating women, unaffected adversely by x-ray treatment, we may include six patients who menstruated with clocklike regularity but had, for a long time (nearly five years), either excessive or prolonged flows. Examination of endometrial tissues excluded the presence of intrauterine pathology other than varying degrees of hyperplasia. The six patients were followed up for periods averaging nineteen months. In none of them was the menstrual rhythm disturbed as a result of the roentgen-ray treatment. Three of the six were cured, 2 were improved, and the condition of one remained unchanged.

From the study of the records of these seventeen regularly menstruating women, we may conclude that x-ray exposures in doses within the limits outlined above do not interfere with the rhythm of the menstrual cycle and that fertility in those who desire and can bear children (six of the group of seventeen) is, at least, not lowered by the procedure. We may also infer that the dysfunctional menorrhagia of cyclically menstruating women is, to a large degree, controllable by this measure.

#### EFFECT ON AMENORRHEA

Of the 51 women in this group, 3 had never menstruated (primary amenorrhea), 12 had no menstrual periods during the year preceding treatment, and 35 had menstruated at intervals of four or more months but less than twelve months. The average duration of the disturbance for the entire group was 5.7 years. Twenty of these patients had received prior to the use of roentgen rays some form of organotherapy without relief.

Only one of the three patients with primary amenorrhea responded and has been menstruating at intervals of four to five weeks for a period of a year. The intensive organotherapy she received months before the x-ray treatment may have contributed to the result by increasing the growth and vascularity of the uterus. Twenty-two of the forty-eight women with secondary amenorrhea have been menstruating regularly for periods of one or more years, averaging 2.3 years; four improved in the form of increased menstrual frequency; sixteen failed to respond; and the remaining six conceived too soon (one to three months) after the roentgen ray therapy to enable us to evaluate its effect on menstrual periodicity. Four of these six women have been menstruating regularly for periods averaging three years since the weaning of their infants. Pregnancy in these four patients undoubtedly contributed largely to the subsequent reestablishment of normal menstruation. Two of the six remained amenorrheic despite the stimulus of pregnancy.

Twenty-three (49 per cent) of forty-seven amenorrheic women have been menstruating regularly for periods of one to four years, an average

of slightly more than two years for the group, without the stimulus of intercurrent pregnancies. There is no other agent at the disposal of the profession capable of producing this result with so little trouble and expense to the patient. One of the sixteen patients who totally failed to respond to treatment was presumably made worse. The intervals between periods became even longer than before treatment. Nine of the fifty-one amenorrheic patients received one or two additional courses of roentgen ray treatment after the first course of three exposures failed to produce more than slight improvement. Five of these nine fully responded to the additional exposures and are included in the group of twenty-three cures.

#### EFFECT ON OLIGOMENORRHEA (MODERATE DELAY IN MENSTRUATION)

Twenty-one patients had menstrual intervals of six to thirteen weeks. This irregularity connotes a milder form of ovarian deficiency, whether primary or secondary, than frank amenorrhea and yields more readily to treatment. The average duration of the menstrual disturbance for the entire group was 7.2 years. Nine of the group had received organotherapy without relief prior to the roentgen ray treatment. Eight of the twenty-one patients in this group have been menstruating regularly for periods averaging nineteen months since the treatment was given; six showed either slight or no improvement; one was presumably, adversely affected by the treatment and menstruated thereafter at longer intervals; six who were previously sterile conceived so soon after the x-ray exposures (one to three months) that the immediate effect on menstrual periodicity cannot be gauged. They have been menstruating regularly, however, for an average period of two years since the weaning of their infants. Excluding these six from our calculation on the assumption that incidental pregnancies contributed to the eventual establishment of normal menstrual periodicity, the percentage of cures in the group of fifteen patients was a little over 50 per cent. Two of the patients required additional courses of treatment, given in three months, before a cure was accomplished.

#### EFFECT ON DYSFUNCTIONAL UTERINE BLEEDING (METRORRHAGIA)

Thirteen women of childbearing age suffering from metrorrhagia of average duration of twenty months were subjected to low-dosage irradiation of the pituitary gland and ovaries. All of them had previously received organotherapy without relief. Ten of these thirteen patients fully responded and have remained well for periods averaging 2.8 years. One improved and two were not benefited by the treatment.

The greater response (80 per cent) of dysfunctional metrorrhagia of the childbearing age than that of amenorrhea confirms our conviction that metrorrhagia is a symptom of a milder form of the same endocrine

defect. In dysfunctional metrorrhagia the lutein phase alone is defective or totally absent, whereas in amenorrhea the ovarian follicle, the predecessor of the corpus luteum, is likewise functionally deficient and fails to produce enough estrin to rebuild the dismantled endometrium of the previous cycle. With this concept of the mechanism of the two seemingly opposing symptoms (an excess and an absence of uterine bleeding), we can readily understand why the same agent is helpful in both and more effective in the former. The only exception to this formula is the occasional case of hyperhormonal amenorrhea, a condition wherein the uterus is incapable of responding to a normal or even excessive supply of the follicular hormone.

#### EFFECT ON ASSOCIATED STERILITY

Sterility was either a primary or an associated factor in the majority of the 103 patients treated. Thirty-eight were married to fertile mates and had no discernible cause to account for the sterility other than disturbances of the menstrual rhythm. Eighteen of the thirty-eight conceived and gave birth to healthy infants; two are pregnant at this time; one aborted before an ultimate successful pregnancy; and another one aborted and subsequently no longer desired pregnancy. We may infer from these figures that correction of the menstrual defects was conducive to pregnancy in half of the functionally sterile woman. A few of the women not desiring pregnancy conceived involuntarily. There was a total of twenty-six live births and three abortions in the irradiated patients. The percentage of abortions is not larger than in those treated by other measures, though considerably larger than that current in normal women. The tendency of women suffering from menstrual disturbances and genital hypoplasia to abort is well known.

#### EFFECT ON PRIMARY DYSMENORRHEA

Fourteen of the 102 patients subjected to low-dosage irradiation had, as an associated symptom, varying degrees of primary dysmenorrhea. This is a rather low incidence in a group of patients, the majority of whom presented definite evidence of genital hypoplasia. We must remember, however, that the majority of these patients presented the stigmas of pituitary deficiency wherein dysmenorrhea, despite the associated genital hypoplasia, is rarely, if ever, a prominent symptom. Dysmenorrhea usually occurs in the primary hypogonadal type of women in whom the associated instability of the autonomic nervous system is apparently the major factor in the causation of menstrual pain. Five of the fourteen patients were relieved of dysmenorrhea when normal menstruation was reestablished; two were relieved by pregnancy that followed soon after irradiation; the dysmenorrhea of the remaining seven was not affected despite the fact that fully six of them were relieved of the associated menstrual irregularity.

## SUMMARY

Twenty-three of forty-seven women suffering from severe amenorrhea have been menstruating regularly without the stimulus of incidental pregnancies for periods averaging 2.3 years following low-dosage irradiation of the ovaries and pituitary gland.

Eight of fifteen women suffering from a milder form of amenorrhea (oligomenorrhea) likewise were restored to normalcy without the aid of incidental pregnancies.

Ten additional patients of the twelve who conceived soon after x-ray treatment have been menstruating regularly for periods averaging 2.5 years.

Ten of thirteen patients of childbearing age suffering from dysfunctional metrorrhagia of long duration were cured by one course of treatment.

Associated sterility was relieved in twenty of the thirty-eight women who had no ascertainable cause to account for the condition other than menstrual disturbances.

Primary dysmenorrhea was an associated symptom in fourteen of 102 patients treated. Five of the fourteen were completely and permanently relieved without the aid of incidental pregnancies.

The menstrual rhythm of seventeen regularly menstruating women was not disturbed by the x-ray treatment. Seven of eleven amenorrheic women responded after a second or third course of treatment given at intervals of three months; the condition of the remaining four was not aggravated by repeated exposures. It is assumed, therefore, that the x-ray treatment was not responsible for the aggravation of the amenorrhea of the two patients who had received only single courses of treatment. Twenty-six healthy children were born to women who had received the treatment. These data indicate that the procedure is harmless.

## REFERENCES

- (1) *Lehmann, P.*: Presse med. 42: 1516, 1934. (2) *Edeiken, L.*: AM. J. OBST. & GYNEC. 25: 511, 1933. (3) *Frank, R. T.*: J. A. M. A. 97: 1852, 1931.

1829 PINE STREET

---

Nicholson and Calatroni: Primary Carcinoma of the Hymen, Bol. Soc. de obst. y ginec. 13: 692, 1934.

The authors state that they could find only two cases of primary cancer of the hymen reported in the literature. Their patient was a forty-eight-year-old woman. Pathologic diagnosis: Epithelioma.

MARIO A. CASTALLO.

## BLOOD LOSS DURING CESAREAN SECTION

WILLIAM J. DIECKMANN, M.D., AND EDWIN F. DAILY, M.D.,  
CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, the University of Chicago,  
and the Chicago Lying-in Hospital)*

**A** KNOWLEDGE of the amount of blood lost during delivery is very often of great importance, as the immediate and future management of the case frequently depends on the volume of the hemorrhage. Reports of the average blood loss vary markedly, which might be explained in part by the methods used in the determinations.

Various comments on the amount of hemorrhage, especially the clotted mixture of blood and amniotic fluid in the suction bottle, during cesarean section focused our attention on this problem. The solution to this problem involved an exact determination of the grams of hemoglobin lost at operation and the conversion of this figure into cubic centimeters of the patient's blood.

Schmid gives an extensive summary of the work that has been done in determining the blood loss at delivery. The figures in most of these reports are based on the measurement of the blood caught in a basin. Another method involves the weighing of all blood-stained linen, washing out of the blood and weighing a second time, the difference between the two representing the blood loss. A third method is the determination of the patient's hemoglobin before and after delivery, assuming that the difference represents the blood loss at delivery.

Williams, in 1919, concluded that the usual blood loss during spontaneous delivery ranged from 100 to 300 c.c. His method was to catch the blood in a basin and measure it.

Calkins reported that in 96 per cent of his patients the blood loss at delivery was less than 600 c.c. The average amount was 179 c.c. in 800 cases. He also measured the blood caught in a basin.

The method of catching the blood at the time of delivery frequently does not give the true value for the blood lost from the patient's circulation. Dieckmann and Wegner have noted that during labor there are varying degrees of blood concentration, which may be intensified by anesthesia. Therefore, the blood lost at delivery, if expressed in terms of hemoglobin concentration taken before the onset of labor, may be more than the volume indicates. This phenomenon may explain certain cases of shock, postpartum anemia or puerperal infection. A postpartum hemodilution with blood loss within normal limits indicates the fallacy of estimating the hemorrhage by determining the differences in hemoglobin concentration.

## METHOD

Venous blood was obtained from the patient before delivery or, if possible, before the onset of labor. The hemoglobin was determined as acid hematin. A 1 per cent standard was made from a solution which contained 13.8 gm. of hemoglobin per 100 c.c. as determined by the oxygen capacity method. Ten grams of sodium citrate were placed in the suction bottle to prevent coagulation. All sponges were put in a basin which contained 1,000 c.c. of 0.1 N hydrochloric acid (10 c.c. of concentrated acid in 1,000 c.c. of water) and allowed to soak. The sponges were rinsed thoroughly in the above solution and wrung out dry by hand at the end of the operation. The solution from the sponges and from the suction bottle were mixed together and made up to the nearest convenient mark for dilution (viz., 2,500, 4,500, 6,000). Ten cubic centimeters of this solution were diluted further in a volumetric flask until it could be matched with the standard.

The following case may be cited as an example:

Patient C., No. 91075. Hemoglobin 12.56 gm. per 100 c.c. of blood. The solution amounting to 5,150 c.c. was diluted to 5,500 c.c.; 10 c.c. of this were diluted to 200 c.c., or 20 times. The standard was set at 20, and the unknown reading was 26.

$$\frac{20}{26} \times 0.00138 \text{ gm.} = 0.001061 \text{ gm. per c.c.}$$

$$5,500 \times 20 \times 0.001061 \text{ gm.} = 116.8 \text{ gm. hemoglobin blood loss.}$$

$$\frac{116.8}{12.56} \times 100 = 930 \text{ c.c. total blood loss.}$$

The ordinary laparotomy pad, consisting of six layers of gauze and measuring 8×16 inches, will hold 150 c.c. of blood; one measuring 16×16 inches will hold 300 c.c. of blood.

We were able to recover 87 to 90 per cent of the hemoglobin from a known quantity of blood. If the sponges were rinsed once and the rinsings added to the solution, we were able to recover 98 per cent. Our results, therefore, are at least 10 per cent too low. The use of a wringer and the determination of the hemoglobin from the iron content would simplify the method.

Gatch and Little used a somewhat similar method in determining blood loss from various types of operations. They reported the blood loss in terms of the patient's blood, but did not determine the hemoglobin loss or the patient's hemoglobin. There were four hysterectomies in their series, with a blood loss ranging from 210 to 310 c.c.

Our figures for the blood loss in cesarean sections, forceps and episiotomies, and spontaneous deliveries are given in Table I. The number of operative and spontaneous deliveries is very small. The amount of the blood loss is so variable due to the many factors accompanying delivery, that a study of a large series of cases would be of no particular value. It is obvious, as would be expected, that the minimum blood loss occurs with spontaneous delivery. The cesarean section series is large enough to warrant some generalizations. The wide range and occasional excessive blood loss are noteworthy.

The average blood loss for all the cesarean sections was 546.7 c.c., and the range was 170 to 1,410 c.c. Four cesarean sections were performed for placenta previa, with an average blood loss of 597.5 c.c. and a range

of 235 to 980 c.c. The blood loss in these cases was due to the bleeding from severed sinuses in the lower uterine segment. A low classical cesarean section would obviate this complication. Three cesarean sections

TABLE I

AMOUNT OF BLOOD LOSS C.C.	METHOD OF DELIVERY		
	CESAREAN SECTION	FORCEPS AND EPISIOTOMY	SPON- TANEOUS
Less than 100		1	4
100- 199	3	4	3
200- 299	2	4	1
300- 399	4	1	
400- 499	4	1	
500- 599	1	2	
600- 699	0	1	
700- 799	1	0	
800- 899	0	1	
900- 999	2		
1,000-1,099	1		
1,100-1,199	1		
1,410	1		
Number of patients	20	15	8
Average per case	538.9	342.3	106.8

were performed for abruptio placentae, with an average blood loss of 763.3 c.c. and a range of 440 to 1,410 c.c. including the hemoglobin content of the clots. The amount of blood which may be lost in a cesarean section performed by an experienced surgeon is astounding. None of the staff realized that the blood loss was more than 700 c.c. in seven out of twenty operations.

TABLE II

NUMBER	INDICATIONS FOR LAPAROTRACHELOTOMY	DATE	BLOOD LOSS HEMOGLOBIN AND VOLUME	HEMO- GLOBIN GM./100	HEMATO- CRIT %
S3110	Placenta previa	11/29/33	115 gm.	11.7	43
		12/ 2/33	980 c.c.	8.4	28
		12/ 7/33		8.8	31
S3191	Abruptio placentae 800 c.c. blood transfusion	11/18/33		10.9	31
		11/21/33	154.4 gm.	9.9	29
		11/27/33	1,410 c.c.	10.0	32
		3/ 7/34			47
S3120	Contracted pelvis	10/30/33		12.6	
		11/ 1/33	116.8 gm.	9.5	26
		11/ 8/33	930 c.c.	9.0	27
		11/21/33		9.9	31
		2/27/34		12.1	42

The duration of labor previous to the cesarean section seems to be a factor in the amount of blood loss. Fifteen of the operations were performed before the onset of labor or within the first ten hours, with an average blood loss of 624 c.c. In five operations in which the duration of labor was over ten hours, there was an average blood loss of 256 c.c. It is obvious that there should be less blood loss after several hours of



labor because the lower uterine segment is more attenuated, the vessels are compressed, and the uterus is more irritable, thus contracting more rapidly after delivery.

The baby becomes a factor only when it weighs less than 2,000 gm., with a blood loss of 440 c.c., or over 4,000 gm., with a blood loss of 592 c.c.

Data for several illustrative cases are given in Table II. Hemoglobin and hematocrit determinations made 72 hours or more after delivery give a more reliable index of the blood loss than those made immediately after delivery. Erythrocyte counts at any time are of much less value than a proper hemoglobin and hematocrit determination.

#### COMMENTS

The following conditions and factors predispose to an excessive blood loss during delivery:

1. A marked anemia due to the lack of sufficient erythrocytes for a proper clot.

2. Prolonged labor because of partial atony of the uterus.

3. Multiparity—usually after the fourth pregnancy, because of faulty contraction of the uterus probably due to fibrosis or other changes in the uterine wall.

4. Overdistention of the uterus from multiple pregnancy, abnormally large baby, or polyhydramnios because of partial atony of the uterus or of the surface area of the placenta. Adair and Thelander have demonstrated a positive correlation between the area of the placenta and the weight of the baby.

5. Episiotomy or laceration of the cervix, vagina or perineum.

6. Improper management of the third stage of labor.

The blood loss may be kept at a minimum by (1) allowing sufficient time for the separation of the placenta, which usually occurs within one to six minutes after delivery; (2) by the expression of the placenta from the lower uterine segment or vagina, using the *contracted* uterus as a piston, and (3) by injecting pituitrin intramuscularly after the expulsion of the placenta.

The following additional conditions predispose to an increased blood loss during cesarean section:

1. Placental site underlying the uterine incision.

2. Rapid delivery of the infant, preventing proper contraction of the uterus.

3. Tears resulting from an inadequate uterine incision.

4. Elective operation and those performed early in labor.

Pituitrin should be injected into the uterine muscle after the head of the infant is delivered, and then after two or more minutes the remainder

of the baby should be slowly extracted. Thus the uterine muscle will have time to accommodate itself to the tremendous decrease in the size of the cavity, and the amount of the hemorrhage will thereby be lessened.

The amount of the blood loss must be correlated with the patient's weight and with her hemoglobin concentration. It is obvious that a blood loss of 1,000 c.c. from a patient weighing 50 kilograms and having a blood volume of 4,000 c.c. is of more serious import than the same amount from a woman weighing 70 kilograms, with a blood volume of 5,600 c.c. Furthermore, if the patient has an anemia or already has lost blood, an additional hemorrhage, even though not excessive, may be just enough to use up the last reserve of hemoglobin and death may result. Dieckmann and Wegner have demonstrated that although the average increase of the blood volume at term is 23 per cent, it is not sufficient to enable the pregnant woman to withstand a large blood loss, as is stated in many textbooks.

At the beginning of our study estimates of the blood loss by various observers were generally 100 to 700 c.c. below the actual amount. Later the difference between the estimated and determined amounts became much less. Thus, this study was of considerable importance in teaching our staff to estimate blood loss accurately, and also made them "hemorrhage conscious."

#### SUMMARY

1. A method for accurately determining the blood loss during delivery or operation is described.

2. The average blood loss in a spontaneous delivery was 107 c.c., in the delivery by forceps and episiotomy 342 c.c., and in the cesarean section it was 539 c.c.

3. Certain factors and conditions governing the blood loss are discussed.

4. Methods are described for the management of the third stage of labor, for delivery through the natural passage, and also by cesarean section.

#### REFERENCES

- Adair, F. L., and Thelander, H.*: AM. J. OBST. & GYNEC. 10: 3, 1925. *Collins, L. A.*: J. A. M. A. 101: 1128, 1933. *Dieckmann, Wm. J., and Wegner, C.*: Arch. Int. Med. 53: 71 and 188, 1934. *Gatch, W., and Little, W.*: J. A. M. A. 83: 1975, 1924. *Schmid, H. H.*: Halban u. Seitz 8: Part 1, 108, Urban & Schwarzenberg, Berlin, 1927. *Williams, J. W.*: Am. J. Obst. 80: 1, 1919.

## THE TREATMENT OF ABRUPTIO PLACENTAE\*

JOHN A. MCGINN, M.D., F.A.C.S., AND W. BENSON HARER, M.D.,  
F.A.C.S., PHILADELPHIA, PA.

*(From the Department of Obstetrics of the St. Agnes Hospital)*

**D**URING recent years a very laudable interest has been shown in efforts to reduce maternal mortality rates. Unfortunately, a reduction in mortality from all causes cannot be hoped for. However, certain conditions offer ripe fields for improvement. Abruption placentae, with its accompanying 40 to 60 per cent maternal mortality, is an outstanding example. This fact, together with our experience in connection with three recent cases of abruption placentae, all ending fatally for both mother and child, has stimulated this presentation.

The etiology of abruption placentae is based purely on theory. All writers stress traumatism, endometritis, diseases of the ovum, emotional states, and toxemia. It is quite possible that we must look to the early development of the placenta for the real underlying cause. This embryologic factor may quite possibly be a paucity of anchoring villi, so that the placenta is from the very beginning only loosely attached to the decidua basalis. Such a placenta, particularly when subjected to the additional pathologic changes that so frequently accompany late gestational toxemia, would naturally be expected to separate from its uterine attachment. It is generally believed to be more than a coincidence that a high percentage of infarction is found in the placenta in cases of gestational toxemia. Unquestionably, a placenta that is the site of large infarcts is less firmly attached to the decidua than is a normal noninfarcted placenta. Furthermore, it has recently been suggested that in the formation of placental infarcts certain toxic substances derived from the splitting of the proteins of the placenta are passed into the maternal blood stream. Although it has not as yet been proved, it is quite possible that among these toxic substances may be histamine, which Hoffbauer has shown will reproduce the exact pathologic and clinical picture of abruption placentae in pregnant animals which possess placentas whose structure is similar to that of man. Whatever may be the exact relationship between the two conditions, it is unquestionably true that the majority of severe cases of abruption placentae occur in association with late gestational toxemia. We stress this point because of its importance in connection with the treatment of abruption placentae.

The signs and symptoms of abruption placentae are so well known that they need not be repeated here. Rather we will take time to discuss

---

\*Read at a meeting of the Obstetrical Society of Philadelphia, January 3, 1935.

certain factors in connection with the pathology of this condition, and the effects of these pathologic changes upon certain of the physiologic functions of the uterus. The first step in the separation of the placenta is hemorrhage into the decidual portion of the placenta. This hemorrhage, small at first, rapidly increases in amount and so forms a retroplacental hematoma which further dissects the placenta from the uterine wall and so constantly opens additional blood vessels and blood spaces, thus increasing the retroplacental hematoma and causing pressure and irritation of the uterine muscle. This pressure of course is exerted equally in all directions but its greatest effect will be manifested in the direction which offers least resistance to its passing. This may be into the uterine muscle itself, into the depths of the placenta and so toward the amniotic sac, into which it may rupture (rarely), or between the uterine wall and fetal membranes and so finally reach the internal os, from which point the blood may escape into the vagina. As a result of the irritation of the uterine muscle, the uterus is usually thrown into a state of tetanic contraction which is maintained until fatigue of the muscle fibers results in a secondary relaxation. During the stage of tetanic contraction the blood vessels and venous sinuses at the site of the placental separation are compressed and further blood loss considerably retarded or even stopped. With the onset of fatigue and the relaxation of the uterus these vessels and venous sinuses again open up and more blood escapes. Regardless of the direction in which the main quantity of blood may be forced, there is always a considerable amount of blood forced into the uterine wall between the muscle fibers and in some cases enough is squeezed through the wall of the uterus to appear as petechiae or even hematomae under the serous coat. Rarely enough may be forced through the uterine wall to rupture into the abdominal cavity. Such extravasations of blood into the myometrium were called placental apoplexy by Couvelair. Let us consider the effect of these extravasations upon the physiologic functions of the uterus. As already stated, the irritation of this blood throws the uterus into a state of tetanic contraction. Such contractions greatly diminish the expelling properties of the uterine muscle so that the progress of labor in such cases is markedly retarded. That this tetanic contraction is distinct from the ordinary uterine contractions of labor is proved by the superimposition of rhythmical labor pains in a uterus which is constantly and continuously in this state of tetanic contraction. As the blood is squeezed into the myometrium it distends the wall of the uterus and separates the muscle fibers, and so greatly interferes with the function of retractsility. It is this function which enables the uterine wall to close down and reduce the uterine cavity as the contents of the uterus are passed out, into and through the birth canal. This function is, therefore, of great importance in the control of bleeding postpartum. Consequently, with the function of retractsility greatly diminished or even com-

pletely lost in abruptio placentae, postpartum hemorrhage is the natural sequel. In the normal uterus the functions of contractility and retractility are so closely coordinated as to be practically indistinguishable. They are, however, separate and distinct functions, as was well illustrated in one of the cases reported in this paper, where the uterus remained in a fair state of contraction following the delivery of the child, but remained larger in size than is normal, thus indicating the loss of retractility.

In the final analysis there is but one object to be considered in the treatment of abruptio placentae, namely, the prevention of further blood loss and the restoration of maternal blood volume. To best attain this object, however, a great number of related factors must be taken into consideration; thus the parity of the mother, the stage of pregnancy, condition of the fetus, condition of the cervix, and the clinical evidence as to the amount of blood already lost, are all of great importance. However, the factor that we desire to stress in this paper is time. The hemorrhage of abruptio placentae is so difficult to control because of the inaccessibility of the source of the bleeding. Furthermore, in those cases in which all or a large part of the placenta becomes detached, the amount of blood lost may be great within a very short time. In such a case with rapidly developing signs of profuse hemorrhage, prompt and energetic treatment is called for. Suitable blood donors must be obtained as quickly as possible and immediate cesarean section performed so as to prevent further blood loss. If necessary, a transfusion may be given before laparotomy is performed, but where the patient's condition warrants it, better results are obtained by withholding the transfusion until the hemorrhage has been controlled. Such cases do not give us a great deal of concern as to the form of treatment to be used. Our judgment is most taxed by those cases that are undoubtedly abruptio placentae but in which the patients show but little clinical evidence of blood loss. In these patients the question comes up whether to employ conservative measures in the hopes of being able to deliver the patient by the vaginal route or to use the more drastic cesarean section. It is this type of case in which the time factor becomes of great importance. In a multipara, with well-dilated birth canal and no disproportion, where labor is already in progress and advancing rapidly, one may well delay active interference for a reasonable length of time. In such cases the blood pressure, cardiac and respiratory rates, must be watched very closely, together with the other clinical signs of internal hemorrhage. As soon as the cervix becomes sufficiently effaced to be readily dilatable, manual dilatation with prompt delivery by version or forceps should be undertaken. Immediately after the delivery of the fetus, the placenta should be expressed and the uterus and vagina firmly tamponed with dry gauze. Pituitrin and gynergen, together with hemostatic serum, should be administered to assist in the contraction and

retraction of the uterus and to increase the coagulability of the blood. Blood transfusion may also be required in such cases. In a primipara with undilated birth canal and in all cases with disproportion or those in which labor is not progressing rapidly, immediate cesarean section will give the best ultimate result. It is not safe to permit any woman in whom a diagnosis of abruptio placentae has been made to remain undelivered for any considerable length of time, even in the absence of clinical evidence of profuse hemorrhage. In such cases, even though the patient may show little or no evidence of continuing blood loss, there is no reliable way of telling how much blood has been squeezed into the myometrium, and consequently no way of predicting how this myometrium will be able to function when the uterus is finally emptied. In these cases, cesarean section is by far the best method of treatment, since it permits us directly to inspect the uterus and to determine accurately the extent of myometrial damage. If sufficient extravasation of blood has occurred in the myometrium, as would in the opinion of the operator tend to prevent the matting together of the muscle fibers and the overlapping of muscle bundles, and to prevent proper retraction of the uterus after it is emptied of its contents, then coincident hysterectomy is indicated. In those cases where hysterectomy is not done the uterus should be firmly tamponed with gauze before suturing. Blood transfusion, injection of pituitrin directly into the uterine muscle, application of external heat, elevation of the foot of the bed, administration of cardiac stimulants, and all other supportive measures are used as indicated. It is our feeling, therefore, that delivery by the vaginal route in cases of abruptio placentae is warranted only when delivery is actually, immediately impending or may be promptly accomplished by the use of an obstetric maneuver. In all other cases cesarean section is indicated and should be looked upon as the only logical method of treatment, rather than be considered radical obstetrics.

#### CASE REPORTS

CASE 1.—Mrs. B. L., aged forty-two, para vii. Last menstrual period began January 10. Her pregnancy proceeded normally until the morning of October 7, at which time she was about thirty-eight weeks pregnant. About 9:00 A.M. she began to have labor pains, and soon after their onset she suffered a severe lancinating pain in the lower abdomen and began to bleed from the vagina. This bleeding continued and her physician was called about 11:00 A.M. Upon his arrival he found that the patient had lost considerable blood externally and showed evidence of additional internal hemorrhage. No fetal heart sounds could be heard and fetal movements were not felt. Immediate hospitalization was advised but the patient refused. Her bleeding continued and finally the doctor packed her vaginally. This, however, failed to control her bleeding. Her condition became rapidly worse, until about 5:00 P.M. when the doctor insisted upon her going to a hospital. The patient was admitted to the Maternity Department of St. Agnes Hospital about 7:00 P.M., unconscious, in profound shock, and practically pulseless. Her temperature was subnormal, her skin cold and clammy. The uterus was greatly distended, globular, and

the fetal parts difficult to palpate. No fetal heart tones or fetal movements could be elicited. Vaginal examination eliminated the presence of placenta previa and confirmed the diagnosis of abruptio placentae. The patient was immediately treated for shock by the application of external heat, elevation of the foot of the bed, firm bandaging of the extremities, and the use of cardiac stimulants. An intravenous injection of glucose and saline was administered and blood taken for typing and cross agglutination. A transfusion of 500 c.c. of citrated whole blood was given immediately and preparations were made for cesarean section. The patient reacted only slightly. She became semiconscious and the pulse could again be palpated with difficulty at the wrist. Realizing that the case was a desperate one, we resorted to the only source that offered any hope of saving her life. Ether and oxygen were administered but she stopped breathing and additional restorative measures, including adrenalin given directly into the heart muscle, had to be resorted to. Respiration was again established and a second attempt made to administer an anesthetic, with exactly the same results as before. With great difficulty respiration was again re-established, but the patient's condition was so bad that she died before even a local anesthetic could be used.

*Comment.*—The time limit for any effective form of treatment had been reached long before this patient was admitted to the hospital.

CASE 2.—R. L., aged twenty-eight years. Patient had late gestational toxemia three and one-half years ago. Labor was induced at the seventh month and patient was delivered of a stillborn fetus. Subsequently, complete studies were made on the basis of which it was decided that she might safely become pregnant again.

Her last menstrual period began April 30, 1934. She progressed normally until early in November when her blood pressure rose to 140/90 and her pulse rate increased to 120. Urine showed a heavy trace of albumin.

At 8:00 A.M., on December 4, the patient was seized with severe, constant pain, in the lower abdomen. She had no vaginal bleeding. She was sent to the hospital immediately. Upon her arrival she was having intermittent pains but the uterus was boardlike and did not relax between pains. A diagnosis of abruptio placentae was made and a consultation held. Blood studies showed no evidence of severe internal hemorrhage. Her blood pressure remained at 140/90 and her pulse rate at 140. She showed no evidence, whatsoever, of shock. Because of these facts and because she was definitely in labor, it was decided to wait for spontaneous delivery rather than to operate. However, complete preparations were made for cesarean section, should the patient's condition require it. A suitable donor was kept in the hospital in the event blood transfusion might be necessary.

About 8:00 P.M., on December 4, the patient delivered herself of a stillborn fetus which was immediately followed by the expulsion of the placenta and several fairly large blood clots. She was given an ampule of pituitrin and one of gynergen and showed no abnormal bleeding. However, the uterus did not retract but remained practically the same size as it had been before delivery. The uterine cavity and vagina were, therefore, tightly packed. The patient seemed to be in fair condition. Within a few minutes, however, blood started to ooze through the packing. A blood transfusion was started immediately and the packing was removed and the uterus and vagina repacked. These measures, together with intravenous injection of calcium gluconate and intramuscular injection of parathormone, failed to stop the bleeding. The patient lost ground very rapidly and died on the table.

It is noteworthy that at no time following the delivery, in spite of repeated doses of gynergen with massage of the uterus, intrauterine irrigation of hot saline and repeated packings, did the uterus contract; it remained essentially the same size as before delivery.

The outcome of this case rather indicates that our judgment was faulty in not resorting to cesarean section immediately upon the patient's admission to the hospital.

CASE 3.—Mrs. A. R., aged twenty-one. Pregnancy normal throughout, until she went into labor at term. Had normal labor pains from 4:00 P.M. until 11:00 P.M. Then had a very severe pain in lower abdomen and noticed violent fetal movements, followed by complete cessation of fetal movements. Her pains continued throughout the night, but no progress was noticed in her labor. Her physician finally decided to send her to a hospital. She was admitted to the Maternity Department of St. Agnes Hospital at 10:00 A.M., Dec. 12, 1933. Examination immediately after admission revealed a tetanically contracted uterus, through which the fetal parts could not be palpated. The presenting part was not engaged. The cervix was thick and undilated. There was no vaginal bleeding but the patient showed clinical signs of internal hemorrhage. The uterine contractions were occurring at intervals of three minutes. A diagnosis of abruptio placentae was made and prompt treatment instituted. Blood transfusion was done and cesarean section started at 1:00 P.M. About two-thirds of the placenta was found to be detached and the uterus was filled with old blood clots. Because of the condition of the myometrium, supravaginal hysterectomy was performed. The patient was in bad condition throughout the operation and died just after she was removed from the operating table.

*Comment.*—Too much time was allowed to elapse between the separation of the placenta and the emptying of the uterus. This woman, a primipara, should have had a cesarean section twelve hours earlier.

#### SUMMARY

The treatment of abruptio placentae offers a ripe field for improvement in its maternal mortality rate.

The possible relationship between late gestational toxemia and abruptio placentae is discussed.

The pathology of abruptio placentae and the changes in the physiologic functions of the uterus in this condition, are considered.

A plea is made for earlier resort to cesarean section in cases of abruptio placentae.

1900 RITTENHOUSE SQUARE

---

Bazan and Roth: Non-Surgical Parturition in Three Cases of Premature Partial Separation of the Normally Situated Placenta, *Bol. Soc. de obst. y ginec.* 13: 526, 1934.

The authors report three cases of premature separation of the placenta, treated by rupture of the membranes and injections of spasmalgine. The three babies died; the mothers recovered.

MARIO A. CASTALLO.



## STUDIES IN GLUTATHIONE

### I. TOTAL AND REDUCED GLUTATHIONE, OXYGEN CONTENT AND CAPACITY, AND CELL VOLUME OF BLOOD IN NONPREGNANT AND PREGNANT WOMEN, WITH SPECIAL REFERENCE TO THE TOXEMIAS OF PREGNANCY

FRED W. OBERST, PH.D., AND E. B. WOODS, M.D., IOWA CITY, IOWA  
(From the Department of Obstetrics and Gynecology, State University of Iowa)

RECENT evidence indicates that glutathione may be intimately concerned in intracellular oxidation because of its facility for taking up and liberating hydrogen. This substance is present in both the reduced and oxidized forms in various tissues and in red blood cells, but not in the plasma.

In view of Rodenacker's<sup>1</sup> findings that the oxidizing power of blood and presumably of the tissues decreases slightly toward the end of normal pregnancy, and in eclampsia falls far below the normal level, it seemed that blood glutathione studies combined with oxygen content and capacity determinations in such individuals might give valuable information. Deficient oxidation has been cited by Hochenbecher<sup>2</sup> as the cause of the lowered bicarbonate reserve of the blood in eclampsia, and Stander,<sup>3</sup> in discussing the significance of increased lactic acid of the blood in eclamptic women, argued that whatever theory ultimately explains the etiology of this disease, decreased or deficient oxidation must be taken into account, since he considers this phenomenon the most fundamental yet discovered.

The purpose of the present study was to determine the concentrations of reduced and total glutathione, the oxygen content and capacity, and the cell volume in the blood of nonpregnant women, in normal women during pregnancy, labor and the puerperium, and in individuals suffering from the toxemia of late pregnancy.

#### SUBJECTS AND METHODS

Blood was obtained from 66 women, of whom 10 were nonpregnant (student nurses and patients on the gynecologic ward with no evidence of disease), 18 were in the late weeks of normal pregnancy, 10 were in labor, 10 were puerperal (four to ten days after delivery), and 18 were patients with toxemia of late pregnancy (8 had eclampsia).

The blood was drawn anaerobically under oil without stasis, and was analyzed immediately for total and reduced glutathione, oxygen content and capacity, and cell volume. Samples were taken both early and late in labor from each of the ten parturient women in order to ascertain the effect of the anesthetic, ethylene with

air or oxygen. Cord blood was drawn nearly simultaneously with the maternal specimen. The blood from the other groups was obtained while the individual was at rest (usually in bed) some hours after the ingestion of food.

The glutathione was determined by the method of Woodward and Fry,<sup>4</sup> according to whom the only blood constituent to interfere is thioneine, which, by their estimate, would produce an error of approximately 3 mg. per cent in the glutathione values.

The cell volumes were determined in duplicate using the Plass and Rourke<sup>5</sup> hematocrit tubes\* rotated at 3,200 r.p.m. for thirty minutes.

The oxygen content and capacity were determined by the manometric method of Van Slyke and Neill.<sup>6</sup> The gas apparatus and technique of Van Slyke<sup>7</sup> were used.

## RESULTS

### GLUTATHIONE

The average values for total and reduced glutathione in nonpregnant, pregnant and parturient women, and in those with the toxemia of late pregnancy, show minor variations (Table I), while the total gluta-

TABLE I

THE AVERAGE VALUES OF TOTAL AND REDUCED GLUTATHIONE CONCENTRATION (MG. PER 100 C.C. BLOOD) WITH OXYGEN CONTENT AND CAPACITY AND CELL VOLUME FOR THE VARIOUS GROUPS OF PATIENTS STUDIED

SOURCE OF MATERIAL	NO. OF PTS.	CELL VOL- UME	GLUTATHIONE			OXYGEN		
			RE- DUCED MG. %	TOTAL MG. %	% IN REDUCED FORM	CON- TENT VOL. %	CAPAC- ITY VOL. %	SATI- RATION %
Nonpregnant	10	40.0	38.6	42.1	91.6	8.3	16.7	51.5
Late pregnancy	18	38.5	39.5	43.5	90.8	8.2	16.6	49.4
In early labor before anesthesia	10	39.4	35.1	38.6	91.0	9.2	17.2	53.5
In late labor during ex- pulsion of fetus	10	40.6	37.6	40.8	92.0	13.3	18.3	72.6
Cord blood	10	52.5	50.3	55.8	90.2	12.0	23.1	51.9
Postpartum (4 to 10 days)	10	37.4	40.0	47.1	85.0	7.1	16.5	43.0
Toxemias of preg- nancy*	10	39.7	36.7	43.5	84.4	11.5	18.2	63.2

\*Four patients with eclampsia and six with nonconvulsive toxemia—See Tables II, A and B.

thione is slightly increased in the puerperal group. The range of values among toxemic patients, including those with eclampsia (Table II), was considerably greater than in other groups. The reduced glutathione concentration in normal individuals usually was more than 80 per cent of the total, but occasionally fell below this figure.

As compared with the first stage of labor, prior to administration of the anesthetic, blood taken at delivery showed an increase in the average total glutathione from 38.6 to 40.8 mg. per cent associated with increases in cell volume from 39.4 to 40.6 per cent and in oxygen capacity from 17.2 to 18.3 volume per cent. Since the changes are proportional and in the same direction, it is assumed that they are due to the blood con-

\*These tubes are manufactured by Metolster-Rickell Company, 40 Wendell Street, Cambridge, Mass.

centration which is known to occur under anesthesia late in labor. In patients four to ten days postpartum the total glutathione had increased from an antepartum average of 43.5 to 47.1 mg. per cent, even though the oxygen capacity was practically unchanged.

TABLE II  
INDIVIDUAL DATA ON PATIENTS WITH TOXEMIA OF LATE PREGNANCY  
A—ECLAMPSIA

CASE NO.	CELL VOL.	GLUTATHIONE			OXYGEN		
		REDUCED MG. %	TOTAL MG. %	PER CENT IN REDUCED FORM	CONTENT VOL. %	CAPACITY VOL. %	SATURATION %
17	34.2	----	----	----	13.3	14.8	89.8
77	38.2	18.7	29.0	64.5	14.4	17.3	83.2
80	39.9	33.0	40.2	82.0	12.9	18.2	70.8
84	30.0	51.6	62.2	83.1	9.4*	19.0	49.5
86	34.2	34.8	39.5	88.1	15.6	17.2	90.6
87	37.2	----	----	----	13.3	16.4	81.1
92	31.5	----	----	----	12.2	14.3	85.4
93	41.0	----	----	----	16.8	20.9	80.4
Aver.	36.9	34.5	42.7	79.4	13.5	17.3	78.8

\*Conv. twelve hours previous to drawing of blood. Had received morphine.

#### B—NONCONVULSIVE TOXEMIAS

23†	38.0	----	----	----	11.6	19.7	58.8
44†	38.5	----	----	----	8.8	16.0	55.0
46†	38.5	----	----	----	13.0	17.6	73.8
73†	44.0	----	----	----	7.6	19.2	39.6
77†	41.5	30.2	34.2	88.3	7.8	18.4	42.4
82†	39.6	52.3	57.3	91.3	8.4	12.2	68.8
75†	43.0	31.3	36.9	84.8	16.7	17.9	93.3
79†	44.5	31.3	39.4	79.4	7.8	20.5	38.0
81†	46.0	38.1	43.1	88.4	16.4	19.5	84.2
85†	31.0	45.8	53.3	86.0	4.6	16.8	27.4
Aver.	40.5	38.2	44.0	86.4	10.3	17.8	58.1

†Preeclampsia. ‡Nephritic toxemia.

NOTE: The oxygen content of venous blood in patients with eclampsia is very much higher than in normally pregnant women. Glutathione values among the pregnant women with toxemia are more variable than among the normally pregnant women, even though the averages in the two groups are about the same.

Cord blood, having an average oxygen capacity of 22.1 volume per cent and a cell volume of 52.5 per cent, showed a total glutathione value of 55.8 mg. per cent, which represents approximately the same amount of glutathione per unit volume of cells as in the maternal blood.

#### OXYGEN CONTENT AND CAPACITY

The oxygen content of venous blood was more variable than any of the other constituents, although it was fairly constant among the nonpregnant and the normally pregnant, representing approximately 50 per cent saturation. Early in labor the percentage saturation rose slightly to 53.3 per cent, but by the time of delivery it had increased to 72.6 per cent, probably due largely to the oxygen administered with the

anesthetic, although the increased rate and depth of respiration may have been accessory factors. After delivery it returned in four to seven days to a low average level of 43 per cent. The cord blood was only 51.9 per cent oxygen saturated, probably because its oxygen content is maintained at approximately the maternal level even though its oxygen capacity is markedly increased by the high level of hemoglobin concentration.

It is noteworthy (Table II-A), that the oxygen content of the blood from eclamptic patients is very much higher than in normal pregnant women, the blood being from 70.8 to 90.6 per cent saturated with oxygen, except in Case 84 in which the sample was obtained twelve hours after the last seizure and following heavy doses of morphine. In three other patients (Nos. 17, 80, and 86), the specimens were drawn immediately following a convulsive attack. Patient No. 77, during the preeclamptic state, showed a blood oxygen saturation of 42.4 per cent, while two days later, forty-five minutes after a single convulsion, the blood was 83.2 per cent saturated with oxygen. Patients with noneconvulsive toxemias (Table II-B) showed marked variations in oxygen content and in the percentage of oxygen saturation. It is suggested that these variations may revolve around alterations in the respiratory and pulse rates.

#### DISCUSSION

These studies on blood glutathione do not support the contention of Rodenacker,<sup>1</sup> and Hochenbechler,<sup>2</sup> which are discussed fully by Stander,<sup>3</sup> that there is a consistently decreased or deficient oxidation in the body tissues of pregnant and toxemic women. The observed glutathione values in the toxemic patients studied do not vary from normal, thus confirming the recent evidence advanced by Stander<sup>4</sup> from a study of six eclamptic women. In general the concentration of total and reduced glutathione varies directly with cell volume but is independent of blood oxygen saturation. In contrast with Stander's<sup>5</sup> observation of a reduced blood glutathione in the early puerperium, our values four to ten days after delivery are higher than those obtained in the nonpregnant or in the late weeks of normal gestation.

The unusually high oxygen saturation of venous blood in eclamptic women may theoretically be due to a decreased or deficient oxidation in the body tissue, but the evidence here adduced argues against such an hypothesis. It is more probable that the rapid respiratory and pulse rates, observed in eclamptics account for the high oxygen saturation, while the high values for maternal blood at the time of parturition are probably due to the high oxygen concentration of the anesthetic mixture. The oxygen saturation of cord blood, drawn nearly simultaneously with the maternal blood at the end of parturition, is practically the same as that of maternal blood drawn early in labor. This might suggest that

oxygen is not readily transported through the placenta to the fetus, but it seems more probable that the low oxygen saturation percentage of fetal blood is related to its much greater oxygen capacity. The oxygen content of fetal blood at birth is slightly lower than that of the simultaneously drawn maternal blood, a variation which may be due to a "drag" in the transplacental passage of oxygen or to a more rapid utilization of oxygen by the fetal structures.

#### CONCLUSIONS

1. No essential differences in the average values of reduced and total glutathione were found among normal nonpregnant, pregnant, or parturient women. Puerperal women presented slightly higher total glutathione values. Patients with the toxemias of late pregnancy also showed values approximately within the normal range. Values of cord blood were significantly higher than those of maternal blood.

2. Insignificant variations in the percentage of oxygen saturation were noted in venous blood of nonpregnant, pregnant, and puerperal women. During delivery, when an anesthetic agent containing oxygen was administered, the average oxygen saturation was increased from 53.5 to 72.6 per cent.

3. In the nonconvulsive toxemias of pregnancy the oxygen saturation was variable but tended to be higher than in the normally pregnant group. In eight women with eclampsia, the average value for oxygen saturation of venous blood was 78.9 per cent; significantly higher than in any other group.

#### REFERENCES

- (1) *Rodenacker, G.*: Zentralbl. f. Gynäk. 51: 1446, 1927. (2) *Hochenbechler, A.*: Monatschr. f. Geburtsh. u. Gynäk. 69: 206, 1925. (3) *Stander, H. J.*: AM. J. OBST. & GYNEC. 12: 633, 1926; 13: 551, 1927. (4) *Woodward, G. E., and Fry, E. G.*: J. Biol. Chem. 97: 465, 1932. (5) *Plass, E. D., and Rourke, M. D.*: J. Clin. Investigation 5: 531, 1928. (6) *Van Slyke, D. D., and Neill, J. M.*: J. Biol. Chem. 61: 523, 1924. (7) *Van Slyke, D. D.*: J. Biol. Chem. 73: 121, 1927. (8) *Stander, H. J.*: AM. J. OBST. & GYNEC. 28: 856, 1934.

## TOTAL VERSUS SUBTOTAL ABDOMINAL HYSTERECTOMY IN BENIGN UTERINE DISEASE\*

EDWARD H. RICHARDSON, M.D., BALTIMORE, Md.

*(From the Department of Gynecology of the Johns Hopkins University and Hospital)*

THE subject of this discourse has been a controversial one for many years. On the one hand, a majority group of conservative pelvic surgeons has consistently maintained emphatic opposition to routine total abdominal hysterectomy, believing that this procedure is indicated only when subtotal hysterectomy does not suffice completely to eradicate uterine disease; while on the other hand, a minority group has vehemently contended that subtotal hysterectomy is in reality an inadequate and unsatisfactory operation to be resorted to only when confronted with exigencies that compel its adoption, since it leaves behind a cervical stump which they assert henceforth constitutes a perennial menace to its possessor.

Notwithstanding the fact that seven years ago I published, and have since actively sponsored, a simplified technic for total abdominal hysterectomy, I have repeatedly voiced my active alliance with the conservative majority in this controversy. But I am frank to confess that lately my own convictions became a bit unsettled through the emulative influence of multiplying reports within recent years of a surprisingly large number of cervical stump cancers together with the fact that, because of these reports, a considerable number of eminent surgeons have been induced to adopt and advocate routine total hysterectomy. Consequently I was stimulated to undertake a comprehensive review of the literature in order to evaluate impartially the factual as well as the inferential data pertinent to this discussion. It is my purpose to present here only a brief synopsis of this study in hopes that it may prove helpful in bringing about greater unanimity, both of surgical teaching and practice as regards the preferential operative treatment of benign uterine maladies.

Perhaps the most cogent argument offered in support of their contention by the advocates of routine total hysterectomy is the apparent steadily mounting incidence of cervical stump cancer. Judging from my own observations alone, extending now over a period of twenty-five years of active clinic work and private practice, I would unhesitatingly conclude that the occurrence of stump cancer is so rare as to be a

\*Read, by invitation, before the Chicago Gynecological Society, Chicago, Illinois, March 15, 1935.

This paper was published in part in the *American Journal of Surgery*, June, 1935 (June issue), having been presented at a meeting of the Southern Surgical Society in December, 1934.

negligible factor in this discussion. Consequently, great indeed was my surprise to learn from a recent publication by Von Graff that he had been able to assemble nearly twelve hundred cases, two-thirds of which have been reported within the last twelve years. Certainly, therefore, cancer of the cervical stump can no longer be considered a rarity. Unfortunately, it is impossible to determine with any degree of accuracy its absolute incidence, because no one has the remotest idea how many thousand subtotal hysterectomies have been performed the world over to produce twelve hundred instances of stump cancer. Nor, on the other hand, is it at all probable that this number represents the total incidence, since scattered cases must have been observed here and there which have never been reported. The average incidence subsequent to approximately ten thousand subtotal hysterectomies reported by a dozen different authors is a little less than 1 per cent. But in a study at the Hopkins Clinic just completed and not yet published Erle Henriksen found among 940 cases of cancer of the cervix an incidence of 2.3 per cent of stump cancer. In some other statistical reports of the same kind this percentage is considerably higher, the average being around 4 per cent. Curiously enough, in the literature on cervical stump cancer both from American and European sources one repeatedly encounters the testimony of men who for years have been either at the head of or closely identified with large and active gynecologic clinics that they have never seen a single case of stump cancer. Such wide statistical variations are to be explained probably by the fact that within recent years most of the cervical cancer cases have been referred for treatment only to institutions which are adequately equipped for irradiation therapy. All factors considered, I do not believe that the actual incidence of stump cancer the world over today exceeds 3 per cent.

In this connection it is important to consider the time interval between the performance of subtotal hysterectomy and the subsequent appearance of stump cancer. Most writers upon the subject have arbitrarily assumed that all cancers becoming manifest within one year were present and overlooked at the time of the operation. Now over 20 per cent of the cases fall into this category. The remainder, constituting more than three-fourths of the total incidence, have developed after periods of from one to twenty years and all of these, according to the claims of its advocates, would have been saved by routine total hysterectomy. Obviously this assertion is entirely unwarranted, since not only does it inaccurately assume that the more radical operation as performed by the average surgeon carries with it no mortality whatsoever, but also it utterly ignores authentic reports of a score or more of vaginal vault cancers which developed subsequent to total hysterectomy, thus proving conclusively that even this procedure does not afford absolute protection.

But the major fallacy in the argument of those who contend that the present incidence of stump cancer is itself reason sufficient for the universal adoption of routine total hysterectomy is the significant fact that absolutely no data are available for determining the condition at the time of the original operation of those cervixes in which cancer later developed. It is fairly safe to assume that most of them occurred in cervixes which at the time of the subtotal hysterectomy presented the familiar picture of old lacerations, hypertrophy, so-called erosion and chronic infection. Certainly it would be very easy to build up convincing circumstantial evidence in support of this assumption. Indeed one of the most striking and convincing facts established through statistical studies on cancer of the cervix is that the incidence of this disease subsequent to complete eradication of benign cervical lesions is almost negligible. And if this be true, the incidence of stump cancer should be construed not as a compelling reason for the universal adoption of routine total hysterectomy, but rather as an index both of reprehensible neglect in the postoperative treatment of diseased cervical stumps and of the unfortunate choice of cases suitable for subtotal hysterectomy. This latter operation is properly applicable to only four types of cases: (1) to those women requiring hysterectomy for benign disease who possess perfectly normal cervixes; (2) to cases where the operative hazard compels the execution of rapid and conservative surgery; (3) to a few cases where for good and sufficient reason it is of paramount importance to preserve the function of menstruation; and (4) to most cases requiring hysterectomy during pregnancy. Before deciding upon subtotal hysterectomy, therefore, it is incumbent upon the surgeon to scrutinize the cervix with particular care, making use not only of intelligent palpation and accurate inspection of it but also utilizing freely such diagnostic aids as the colposcope, the Schiller test, biopsy, and diagnostic curettage. Furthermore, remembering how frequently coexisting carcinoma at and above the level of the internal os is overlooked, the body of the uterus immediately upon its removal by subtotal hysterectomy should be laid wide open so as to permit accurate inspection of every centimeter of the endometrium; likewise all fibroid tumors should be bisected and carefully examined and an immediate frozen section report should be obtained from any suspicious areas. There is scant likelihood that stump cancer will later develop in any cervix which survives the rigid application of these tests.

Much has been written concerning the predisposing influence upon the development of cancer of the uterus which appears to reside in fibroid tumors. Of course it has long been known that with at least 3 per cent of them there coexists malignant disease in the form of adenocarcinoma of the uterine cavity, sarcomatous degeneration of the fibroid tumors themselves or cancer of the cervix. But recent statistical studies



of uterine cancer reveal the striking fact that cancer of the body occurs nine times and cancer of the cervix four times oftener in association with fibroid tumors than is the incidence in otherwise normal uteri. Moreover, fully two-thirds of the cases of stump cancer thus far reported have followed subtotal hysterectomy for fibroid tumors. Here it should be recalled that there is uniformly associated with fibroid tumors a marked grade of hypertrophy and hyperplasia of the endometrium and that according to some pathologists, the squamous epithelium of the cervix exhibits similar signs of growth activity. Evidence is accumulating which shows an enormous concentration of the ovarian hormone follicleulin in fibroid tumors, a fact which strongly supports the speculative assumption that such colossal cell proliferation as is exemplified in a rapidly growing fibroid tumor, and contemporaneously both in the hyperplasia of the endometrium and possibly also in the squamous cells covering the portio vaginalis, must be the direct result of sustained and powerful stimulation of a growth hormone. Whether or not such dysfunctional hormonal influence is responsible for an epithelial transition particularly favorable to the later development of cancer is but one of a number of related problems that await solution through the energetic and untiring efforts of our esteemed research colleagues.

The practice of coring out the mucous membrane of the cervical canal at the time of subtotal hysterectomy or destruction of it by heat applied in one form or another has been emphasized by some surgeons and adopted by a considerable number as a reliable safeguard against the subsequent development of stump cancer. But when it is recalled that more than 80 per cent of all cancers of the cervix originate from the squamous epithelium of the portio vaginalis it becomes evident that this procedure has only a meager prophylactic value. On the other hand, the majority of stump cancers appearing within one year after subtotal hysterectomy are adenocarcinomas, and since these are assumed to coexist at the time of the operation, it becomes evident that the block of cored out cervical tissue possesses particular value for immediate biopsy by the frozen section technique.

Two other points of practical importance appear to have been established through statistical studies which need to be emphasized because they are in conflict with prevailing surgical opinion; (1) that approximately 10 per cent of these stump cancers occur in women from twenty to thirty-five years of age; and (2) that over 20 per cent of these women have never been pregnant.

The latter point serves to focus our attention sharply upon the possible rôle which chronic infections of the cervix play in the etiology of cancer, since a considerable proportion of stump cancers follow subtotal hysterectomies performed because of the late consequence of uterine and adnexal infections. Furthermore, it has been abundantly demon-

strated that such infected cervixes are etiologically responsible for at least a small proportion of the cases of infections arthritis. Chronic leucorrhea, which is so prevalent as to be accorded but scant consideration by the average doctor, is the sign that points unmistakably to the existence of these lurking menaces. Consequently, the teaching of those who emphatically condemn subtotal hysterectomy in the presence of chronic infection of the cervix is unquestionably sound.

Conspicuous in all of the discussions upon the universal adoption of routine total as distinguished from elective total hysterectomy has been the question of relative mortality. Unfortunately, on this phase of the subject statistics prove their own unreliability. Where they represent the operative results of highly trained, experienced and skillful surgeons the percentage difference in mortality between the two operations is so small as to represent only the accidents common to all branches of major surgery. In such hands the mortality in either group does not exceed 1.5 per cent. But, according to the statistics of Fullerton and Faulkner based on 1,851 consecutive hysterectomies, where the figures apply to the average run of an active clinic in which the routine operating over a period of years has been participated in by a score or more of individuals, including senior residents who have not yet completed their apprenticeships, the gross mortality in both types of hysterectomy is 4 to 4.5 per cent. Note, however, that in 63 per cent of 1,078 total hysterectomies performed by five members of the visiting staff the mortality was 3.5 per cent; while in 37 per cent performed by twenty members of the resident staff the mortality was 5.2 per cent. These figures indicate clearly enough what would happen if inexperienced pelvic surgeons everywhere undertook the routine performance of total hysterectomy.

Furthermore, comparison of mortality statistics alone by no means tells the whole story. Certainly consideration of postoperative complications and of morbidity should not be omitted when one undertakes to evaluate the relative merits of two operative procedures. Notwithstanding this fact, there is a striking and disquieting paucity of data in the literature relating to this vitally important phase of the subject. But from my own observation and experience I have no hesitancy in asserting that if such specific tests as the incidence of operative and postoperative hemorrhage, surgical shock, damage to bladder, ureters and rectum with consequent fistula formation, postoperative cystitis, pelvic cellulitis, peritonitis, intestinal obstruction, wound infections, phlebitis, thrombosis and embolism, pneumonia, sustained daily elevation of temperature above 100° and total duration of convalescence were rigidly applied, it would be exceedingly difficult to justify the advocacy of universal routine total hysterectomy. Unquestionably this is a surgical procedure of far greater

magnitude requiring larger experience and more highly developed technical skill for its successful application than does subtotal hysterectomy.

A discussion of vaginal hysterectomy does not come within the scope of this paper and I refer to it only to emphasize the fact that in properly selected cases it possesses distinct advantages over both total and subtotal hysterectomy performed by the abdominal route.

From what has been said it is apparent that the advocates of routine total hysterectomy offer three major arguments in support of their contention; (1) the present incidence of stump cancer; (2) the prevalence of focal infections in the cervix; and (3) the assertion that the difference in mortality between total and subtotal hysterectomy is so slight as to be a negligible factor.

Opposing conservative opinion, on the other hand, contends that the incidence of stump cancer should be interpreted merely as an index of the ill-advised use of subtotal hysterectomy or of neglect in the subsequent eradication of benign cervical stump lesions, since one cannot discover in the recorded data any evidence that normal cervices later become cancerous; (2) that in the hands of the average operator total hysterectomy is unquestionably a more hazardous undertaking and is attended by a substantially higher mortality than is the subtotal operation; and (3) that likewise panhysterectomy involves far greater risk of serious operative and postoperative complications, as well as a longer period of morbidity, than does the supracervical technic.

Finally, no one can review the voluminous literature on this subject without being profoundly impressed by the continued reprehensible prevalence of benign diseases of the uterine cervix and their undoubted etiologic relationship to cancer. It is encouraging, however, to note that there now appears to be a real awakening of interest in this matter and that obstetricians generally are beginning to realize the importance of puerperal gynecology. Recent reports from some of our best obstetric clinics reveal that late follow-up examinations disclose unsatisfactory conditions of the cervix and lower birth canal in from 50 to 75 per cent of women who have borne one child or more. And if this be true of the work of expert obstetricians conducted under the most favorable conditions, one can readily understand why it is exceptional to find a normal cervix in conjunction with the indications for hysterectomy. Consequently, despite its many advantages, it is lamentably true that conservative subtotal hysterectomy has today only a limited field of application. And it was recognition of this situation coupled with unsatisfactory experiences with the older operations that led me tediously to develop and seven years ago to publish<sup>1, 2</sup> my simplified technic for abdominal total hysterectomy designed specifically to guard against the major hazards incident to this procedure; namely, mortality, hemorrhage,

shock, damage to ureters, bladder and rectum, and postoperative peritonitis. Thus far in my own series, which as yet totals not quite one hundred cases but which embraces every variety of both simple and complicated pathology requiring this type of surgical therapy, none of these hazards has materialized. Therefore, I can with great confidence heartily recommend this simplified technic to other surgeons who, like myself, have found the older operations formidable and unsatisfactory.

## REFERENCES

- (1) J. A. M. A. 90: 596, 1928. (2) Surg. Gynec. Obst. 48: 248, 1929.

9 EAST CHASE STREET

## A REVIEW OF 190 CASES OF HEART DISEASE COMPLICATING PREGNANCY\*

BERNARD J. HANLEY, M.D., AND JAMES F. ANDERSON, M.D.,  
LOS ANGELES, CALIF.

*(From the Department of Obstetrics and Gynecology, University of Southern California Medical School)*

THIS paper represents a study of 190 cases referred to the Cardiac Clinic of the Los Angeles Maternity Service during the years 1931, 1932, and 1933. These cases represent Negroes, Mexicans, and Caucasians, most of which are of the lowest social order, and, as may be imagined, a great number of these have a very low intelligence quotient. Therefore, it gives an idea of what may be expected from cardiac supervision of cases of this type.

The method of study is as follows: The patient is referred to us because routine examination disclosed a murmur, apparent enlargement, or history of heart disease. A careful history is taken for possible etiology, and she is questioned as to previous evidence of heart disease and the severity of manifestations prior to pregnancy. She is then examined, classified, and instructed as to what change, if any, is necessary in her mode of living. If history and physical examination are not sufficient for diagnosis, she is sent to the General Hospital for orthodiagram, E.K.G., and whatever laboratory work may be necessary.

If the diagnosis is functional heart disease she is returned to her original clinic with instructions to be sent back to us if additional symptoms appear. If organic heart disease is diagnosed, etiologic and structural type is recorded, and she is classified as to function, according to the ability of the heart to withstand ordinary physical activity of the housewife. Class I includes the women able to carry on this work without symptoms. Class II-A are those who are slightly limited, and

Class II-B those who are greatly limited in their ordinary activities. Class III includes those who are able to do no work, or have failure when at rest.

The difficulties encountered in the diagnosis of heart disease in the pregnant woman are increased by several factors, among them being the more rapid heart rate, increased general weight, increased size of hearts, and raised diaphragm with rotation and displacement of the heart. Also many normal pregnant women complain of dyspnea on exertion, fatigue, palpitation and swelling of the ankles. Thus, if murmurs and abnormal valve sounds are present, the patient may show objective and subjective signs of heart disease and still have a normal heart.

This series, comprising 190 cases, was referred to the cardiac clinic from a total of 14,700 seen in the general service. Of these, 125 were classed as functional and 65 as organic. This represents an incidence of 0.44 per cent for the organic group and 0.85 per cent for the functional group. This is a much lower incidence than that of similar groups reported from eastern hospitals.

Let us consider the functional type first. One hundred and six of these showed functional murmurs. These appear as systolic murmurs of all degrees. Most often they are heard over the mitral area, but may be heard over the pulmonic area or both areas. In this series, 52 showed murmurs heard best in the mitral area, 38 in the pulmonic area, and 16 in both areas. Many also showed a very loud third sound, the frequent occurrence of which could not be explained.

The balance of the functional cases consisted of those with histories of frequent palpitation, tachycardia, either paroxysmal or of considerable duration, frequent premature beats, and those who had been told they had heart disease because murmurs had been found in the past, but who had none when examined by us.

The organic group of 65 is for the most part made up of cases of rheumatic heart disease. In it are 49 cases of mitral stenosis, 3 of mitral regurgitation, 1 mitral stenosis plus aortic regurgitation, 1 aortic regurgitation, 2 hypertensive hearts, 2 of syphilitic heart disease, one patent ductus arteriosus, 3 thyroid hearts and one case of hyperthyroidism superimposed on an old rheumatic mitral stenosis of mild degree. We also include in this group 2 myxedema hearts. Thus, as in other series reported, rheumatic heart disease accounts for by far the greater number of cases giving trouble during pregnancy.

In this group, 14, or 21 per cent, had a history of previous failure, and 21, or 32 per cent, had some degree of failure before term. However, failure was usually detected early, and most cases were carried successfully to term. Of the 14 patients who had had previous failure, 7 developed failure before term. The rheumatic hearts accounted for all of the failures except 5. But in terms of percentage, the incidence of failure in the nonrheumatic group was high. One of the thyroid hearts failed and another patient had a thyroidectomy at four and one-half months because of progressive increase in symptoms. The rheumatic plus thyroid case accounted for one of our deaths. One of the 2 hypertensive hearts and both of the syphilitic hearts developed failure. The myxedema hearts, as was expected, improved under treatment and followed uneventful courses.

All of the patients with organic heart disease are examined every two weeks. Pulse rate and blood pressure are taken, and the patient is examined physically. The earliest signs of failure should be recognized. These are, in our opinion, persistent râles at the bases of the lungs and an increase in pulse rate. Changes

in respiration, cyanosis and edema appear later. We feel that the foregoing observations on a patient, with which one is familiar, are of more value than standardized effort tests, and determination of vital capacity in determining when the heart is reaching the limit of its reserve. Reduction of activity or absolute rest is ordered on the impression that the patient gives following physical examination and questioning as to the amount of physical effort indulged in since the last visit, and her reaction thereto.

The progress of the patient under observation, as well as age, pelvic measurements, number of previous pregnancies and behavior in them all enter into recommendations for delivery. When the cardiac reserve is well maintained and measurements normal, she may even be delivered at home, but when the reserve is low, it is recommended that she be hospitalized for delivery.

Of these 65 cases of organic heart disease complicating pregnancy, it has been possible to get complete records on 53, 81 per cent. These are divided as follows: Class I, 15 cases; Class II-A, 18 cases; Class II-B, 19 cases; Class III, 1 case.

There were 12 patients delivered in their homes and 41 in the General Hospital. A follow-up on all of these cases was made from six weeks to three years post-partum. In Tables I to IV the cases are separated into primiparas and multiparas for purposes of comparison as to the length of labor, methods of delivery, and weight of the baby. Practically all patients had some type of analgesia during labor.

TABLE I. CLASS I

	PRIM.	MULT.
Cases	6	9
Type of Delivery		
Spontaneous	5	8
Low forceps	1	0
Version extraction	0	1
Av. length first stage	8.5 hr.	8.5 hr.
Av. length second stage	1.5 hr.	0.5 hr.
Av. weight of baby	6.5 lb.	7.5 lb.

Class I, of course, represents the most favorable type of organic heart disease complicating pregnancy. All these cases were delivered through the birth canal. All patients were discharged in good condition and were found to be in good condition in the follow-up.

TABLE II. CLASS II-A

	PRIM.	MULT.
Cases	5	13
Type of Delivery		
Spontaneous	3	8
Low forceps	1	0
Midforceps	1	0
Version extraction	0	1
Cesarean section	0	4
Av. length first stage	11.0 hr.	7.5 hr.
Av. length second stage	0.75 hr.	0.75 hr.

All patients in Class II-A were discharged in good condition. One patient showed evidence of heart failure in the follow-up.

All primiparas in Class II-B who were delivered were discharged in good condition. One showed evidence of heart failure in the follow-up. One primigravida died undelivered. Of the multiparas, ten were discharged in good condition, one died four days postoperative. On the follow-up eight were in good condition and two showed evidence of heart failure.

The patient in Class III left the hospital in fair condition, but died four months postoperative.

TABLE III. CLASS II-B

	PRIM.	MULT.
Cases	8	11
Type of Delivery		
Spontaneous	4	8
Version extraction	1	0
Cesarean section	2	3
Died undelivered	1	0
Av. length first stage	7.5 hr.	9.5 hr.
Av. length second stage	0.75 hr.	0.75 hr.
Av. weight of baby	5.5 lb.	6.5 lb.

TABLE IV. CLASS III

	PRIM.	MULT.
Cases	0	1
Type of Delivery		
Cesarean section	0	1

TABLE V. SUMMARY OF DELIVERIES

Total number of cases	53
Methods of Delivery	
Spontaneous	36
Low forceps	2
Midforceps	1
Version extraction	3
Cesarean section	3
Cesarean section and sterilization	6
Cesarean section and hysterectomy	1
Died undelivered	1

TABLE VI. ABDOMINAL DELIVERIES

AGE	PARA.	INDICATION	ANESTHESIA
39	ii	Previous section and heart	Ethelene
24	0	D. D. S. and heart	Local
35	v	Decompensated heart	Local
20	i	Previous section and heart	Local
30	iii	Toxemia of pregnancy and heart	Spinal
31	0	Ankylosis of hip and heart	Ethelene
28	i	Decompensated heart	Ethelene
41	i	Essential hypertension and heart	Ethelene
25	ii	Heart failure	N2O-Ether
25	i	Previous section and heart	Ethelene

Of the methods of delivery, 10 patients required abdominal section, 7 of which were sterilized. Two primiparas were not sterilized because it is against the policy of the Hospital to sterilize at the first operation unless there are grave reasons. One multipara was not sterilized due to refusal to sign the consent.

No complications developed with the patients shown in Table VI terminated through abdominal surgery. Nine patients were discharged in good condition and one in fair condition.

#### MORTALITY

There were three deaths in this series, giving a mortality rate of 5.5 per cent. A brief summary of each case follows:

CASE 1.—White, aged thirty, para 0, gravida ii; patient first seen in Maternity Clinic Feb. 2, 1933 when about six months pregnant. Past history reveals one spontaneous abortion at four and a half months in 1930; diphtheria and measles in early childhood, influenza in 1918; patient also stated that she had had a paralytic stroke in 1932 but had made a complete recovery shortly thereafter.

Physical examination showed all findings to be within the range of normal except a heart condition which was described in Heart Clinic as advanced mitral stenosis. Patient was advised to take rest periods both morning and afternoon and was given one grain pulverized digitalis each day. Patient seen again at Maternity Clinic on Feb. 17, 1933, at which time she showed evidence of congestive heart failure, and was admitted to the Medical Service at General Hospital the same day, for observation. Patient treated with absolute bed rest, digitalis, and sedatives. However, she made only slight improvement and on February 27 had a sharp pain in her chest after which she became cyanotic and died. There was no autopsy. It was the impression of her attending physician that she had had a pulmonary embolus.

CASE 2.—White, aged forty, para v, gravida ix; first seen in Maternity Clinic June 6, 1931. Past history reveals all previous deliveries to have been spontaneous and three spontaneous abortions. Patient had a thyroidectomy in 1919. She had been well until her last pregnancy in 1927 when there was evidence of heart failure.

Physical examination showed some exophthalmos, a large adenoma of the thyroid, heart was fibrillating, and there was moisture in the bases of both lungs; pregnancy was advanced to about six lunar months. Patient was admitted to the General Hospital immediately, with a diagnosis of recurrent thyrotoxicosis and cardiac decompensation complicating pregnancy. She was treated on the Medical Service and improved under treatment until July 1, 1931, at which time her heart had compensated, and it was felt best to terminate the pregnancy. This was attempted by castor oil, quinine, and nasal pituitary pack, which was unsuccessful. On July 3, a Voorhees' bag was inserted and was expelled twenty-four hours later, followed by a two-pound eight-ounce fetus. Patient went into immediate shock with considerable hemorrhage. It was the opinion of the attending physician that she probably had a ruptured uterus so a laparotomy was advised. A hysterectomy was performed under local anesthesia. There was no evidence of a uterine rupture. Patient was treated for shock by transfusion but died five days later from cardiac decompensation.



six weeks, during which time her heart condition improved. She was seen again at the Clinic at weekly intervals from April 2 to May 5, at which time a cesarean section and sterilization was done at the onset of labor. Patient was discharged from the hospital fourteen days postpartum in fair condition, and was seen again in the Clinic on May 28, 1931, at which time she showed considerable edema of both ankles and complained of dyspnea. Bed rest was advised, and she improved and was up and about two weeks later, however, still complaining of shortness of breath. She suddenly died Sept. 2, 1931; death probably due to pulmonary embolus.

#### SUMMARY

1. A large series, with very low incidence of organic heart disease is reported. We believe that this is due to the small amount of rheumatic fever seen in Southern California.

2. Of these 190 cases, 65 were organic hearts, of which number we were able to get complete records on 53, or 81 per cent.

3. Of these 53 cases of organic heart disease, spontaneous delivery occurred in 68 per cent; forceps delivery in 5.6 per cent; version extraction in 5.6 per cent; cesarean section in 18 per cent. One patient died undelivered. There were two other deaths in this group, making a mortality rate of 5.6 per cent.

4. We believe that careful supervision is of great value in heart disease complicating pregnancy, and with such supervision it does not constitute a serious complication.

5. Abortion was not advised on any cardiac case seen in the Maternity Clinic during this time.

The authors wish to thank Dr. Lyle G. McNelle, Director of the Los Angeles Maternity Service, for permission to use the records.

---

Mascall, W. Neville: The Pathological Diagnosis of Female Gonorrhea, *Lancet* 2: 233, 1933.

The author employed smears, cultures, and complement fixation tests in 500 consecutive cases of gonorrhea to determine the relative value of each diagnostic method.

The "smears" were taken from the urethra and cervical canal and stained according to Jensen's modification of Gram's stain. Only 9.8 per cent of the 500 patients "were positive in smears only." Urethral and cervical cultures were taken routinely on hydrocele agar (pH 7.5), which was previously warmed to 37.5° C. and then incubated at this temperature. Oxidase reactions helped to locate gonococcal colonies. Cultures alone were positive in 31.2 per cent.

The percentages of positives for cultures, fixation tests and smears were 66.8, 58.6, and 45.4 per cent, respectively.

In doing the complement fixation tests, cross-fixation reactions are rare but possible. This test may be positive for three or four months after a clinical cure or may not become positive if treatment is begun early in the disease. By using all three methods, however, only a minimal error will exist, especially since the diagnosis should not be established by the clinical appearance alone. Positive smears and/or cultures are dependable.

H. CLOSE HESSELTINE.

## THE PRIMIPAROUS PERINEUM AFTER FORCEPS DELIVERY\*

A FOLLOW-UP COMPARISON OF RESULTS WITH AND WITHOUT EPISIOTOMY

FRED B. NUGENT, M.D., READING, PA.

*(From the Philadelphia Lying-In Hospital)*

SINCE episiotomy was first suggested by Ould in 1742 this procedure has been the subject of controversy. The first favorable notices came from Michaelis in 1799. Carl Braun gave the operation its name in 1857 only to condemn it as inadvisable and unnecessary. Anna Broomall brought the procedure to American attention in 1878. Stahl in Chicago used perineotomy extensively during the last years of the nineteenth century. In Philadelphia, Barton Cooke Hirst was an early advocate of episiotomy in selected cases. Brooke Anspach's paper in 1915 introduced a series of discussions ending temporarily in Pomeroy's presentation before the American Gynecological Society in 1918. Among the adamant opponents of perineotomy, J. Whitridge Williams was the most outstanding.

Cameron has described episiotomy as "the substitution of a clean cut of definite size where it can do no harm, for a ragged tear of indefinite size where it may cause immediate harm and subsequent injury." In this paper the term episiotomy is used in its broader sense to include all the forms of perineal dissection.

Opinions for and against episiotomy have been formed on the basis of individual experience, but no statistical evidence has been compiled to support the claims of either side. It is the purpose of this paper to analyze the immediate and late results of forceps delivery in 202 primiparas at term, to compare the results with and without episiotomy, and to suggest the need for further study in certain subgroups. In this series those patients were subjected to episiotomy in whom the obstetrician thought a second-degree or greater laceration was unavoidable. Conversely, in those patients delivered without episiotomy no major lacerations were expected. The deliveries, with very few exceptions, were done by internes and residents under supervision. We feel that the results should represent those of the average physician working under optimum hospital conditions.

The general comparison of the two groups shows 130 cases with episiotomy as opposed to seventy-two cases without episiotomy. The age range and average age are entirely comparable. As might be expected

TABLE I. GENERAL COMPARISON OF THE TWO GROUPS

	WITH	WITHOUT
Number of cases	130	72
Age range	15 to 37	13 to 31
Average age	21.5	21.1
Average duration first and second stages	18 hr. 6 min.	13 hr. 54 min.

the duration of labor is longer in the group subjected to episiotomy. This confirms the indications for episiotomy and the more frequent incidence of complicated operative obstetries shown in Table I.

TABLE II. TYPES OF FORCEPS DELIVERY

	WITH	WITHOUT
Midforceps	9.2%	4.2%
Bill maneuver	3.1%	0.0%
Scanzoni maneuver	3.8%	4.2%
After-coming head	2.3%	1.4%
Low forceps	81.6%	90.2%

Of the low-forceps deliveries the large majority in both groups were "prophylactic."

TABLE III. MORBIDITY (OLD BRITISH STANDARD)

Total morbidity (entire group)	21.8%	
	WITH	WITHOUT
Total morbidity	25.4%	15.2%
Low forceps alone	25.0%	17.0%
Morbidity (pyelitis excluded)	20.5%	13.9%

The combined morbidity of both series compares favorably with Stander's total morbidity of 35.4 per cent in 1,000 cases of forceps delivery. There were no maternal deaths in this series. A comparison of our two groups shows a decided increase in the morbidity in the episiotomy series. We have tried to explain this increase upon the basis of the difference in complicated operative incidence, the difference in incidence of intercurrent infection, and the difference in duration of labor. Plass reports a morbidity of 29 per cent in low forceps, 42.2 per cent in mid-forceps and 50 per cent in high forceps. In our series the comparative morbidity of low forceps alone corresponds to the general morbidity in each of entire groups. We had nine cases of pyelitis in the combined groups, seven of which followed the delivery of patients who had been victims of a grip epidemic current during February and March, 1934. Elimination of this single factor of intercurrent infection brought the morbidity in the two groups to 20.5 per cent with episiotomy and 13.9 per cent without.

TABLE IV. EFFECT OF DURATION OF LABOR ON MORBIDITY

	WITH	WITHOUT
Up to 10 hr.	20.9%	18.7%
10 to 20 hr.	27.2%	20.0%
20 to 30 hr.	29.2%	0.0%
30 hr. and up	27.7%	0.0%

Although the morbidity in prolonged labor is higher than in short labor, the same disproportion in favor of the series without episiotomy is present. Considering the morbidity from these three prime angles we must conclude that there is a substantial increase in morbidity attributable to episiotomy.

Episiotomy includes many types of perineal incision. In 1836, von Ritgen advocated many small incisions in the perimeter of the vaginal ring. DuBois in 1847 is credited with first suggesting the oblique incision now known as the mediolateral episiotomy. It was in Gustav Braun's clinic in Vienna that Broomall observed and reported the use of median episiotomy. In 1895, Dührssen introduced the lateral episiotomy favored by Seanzoni.

In our technic the perineum is first thoroughly "ironed out" manually, the forceps are applied and the head drawn against the perineum firmly. Pomeroy called attention to the danger of producing a laceration before episiotomy was done either by waiting too long or by pulling too firmly against the perineum. The incision is made with blunt scissors, severing the perineal structures as deeply as seems necessary to permit delivery of the head without further laceration.

TABLE V. EXTENSIONS

Mediolateral episiotomy		84.6%
Sulcus	8.2%	
Third degree	0.9%	
Median episiotomy		15.4%
Sulcus	5.0%	
Third degree	10.0%	

In 84.6 per cent of the cases mediolateral episiotomy was done. That oblique was elected in which the long axis of the head lay, i.e., right oblique in L.O.A., etc.; 15.4 per cent of cases were subjected to median episiotomy or, more properly, perineotomy. In the mediolateral group (110 cases) 8.2 per cent of cases showed an extension of the incision into the sulcus, while 0.9 per cent showed an extension which involved the sphincter. In the median group (20 cases) 5 per cent showed extension of the episiotomy into the sulcus and 10 per cent showed a third-degree laceration. By definition, in our clinic, any laceration which involves the sphincter, even though only the sphincteric fascia is injured, is designated a third-degree laceration. In none of the cases listed did the laceration extend into the rectal mucosa. This series is too small to be conclusive, but it supports the widespread belief among the profession that if a major laceration is unavoidable it is much safer to elect a mediolateral episiotomy, despite the protection offered by the Pomeroy technic of ironing out the sphincter and placing a mattress suture just above it. The mediolateral episiotomy is more difficult to repair, but as our experience grew the results became entirely comparable.

There are more methods of repair than there are episiotomies. In our clinic two were used. Most frequently a continuous vaginal suture with interrupted sutures in the perineal body where necessary and subcuticular skin closure were used. In cases where unusual trauma, excessive edema of the tissues, or both occurred, interrupted sutures were used throughout. In both methods No. 2 chromic catgut was the only suture material employed. In the series there was one perineal breakdown requiring secondary suture. This occurred on the fourth postpartum day in a patient in whom the interrupted method had been employed. The secondary repair was done on the eighth postpartum day with interrupted silkworm gut sutures.

The lacerations produced in those patients in whom no episiotomy was done, follows:

TABLE VI

"None"	37.5%	Second degree complicated	4.2%
First degree	23.7%	With anterior wall laceration	2 cases
Second degree	27.8%	C. bilateral sulcus laceration	1 case
Third degree	1.4%		
Anterior wall	5.4%		

Williams acknowledges 66.6 per cent of lacerations involving the fourchet in primiparas. Polak in his series found pelvic floor injuries in 34 per cent of primiparas. The chart from our series indicates the known amount of damage found at examination immediately after delivery. As we shall show later, this by no means indicates the true amount of injury. Attention is called to the anterior wall lacerations. These did not occur in the series in which episiotomy was done. The episiotomies and lacerations represent the immediate perineal results of forceps delivery.

In the consideration of the late perineal results of both groups we have used the word perineum in its broadest sense to include three elective anatomical divisions, the anterior and posterior vaginal walls and the outlet. All examinations on which the subsequent report is based were made six weeks postpartum, in as critical a manner as possible by a single examiner. For purposes of classification the results were grouped under three grades.

Grade A, that pelvic floor and perineum which in the judgment of the examiner six weeks postpartum represented as complete a *restitutio ad integrum* as it was possible to attain. Many of this group showed minor relaxations but there was no gaping of the vulva and no bulging of the anterior and posterior vaginal walls on straining.

Grade B, that pelvic floor and perineum which showed a minor failure of restoration in one of the anatomical divisions with good results in the other two.

Grade C, that pelvic floor and perineum which showed a minor failure of restoration in two anatomical divisions, or a major failure in any one of them.

The results are as shown in Table VII.

TABLE VII

	WITH	WITHOUT
Grade A	73.9%	55.6%
Grade B	24.6%	34.7%
Grade C	1.5%	9.7%

This analysis is revealing particularly in the comparison of the Grade C or definitely unsatisfactory results. Grade B is equally important when we consider that in succeeding pregnancies these minor injuries are bound to be increased.

Study of the symptomatic evidence of injury immediately after delivery showed 13 per cent of bladder symptoms in the series with episiotomy as opposed to 16.6 per cent of bladder symptoms in those without it, eliminating pyelitis and cystitis of infectious character from both series. No satisfactory criteria of symptomatic evidence could be established for vaginal outlet and posterior wall study.

Analysis of the results in the three elective anatomical divisions was interesting in its support of episiotomy. In Table VIII the heading "relaxation" appears. In many cases there was a demonstrable anatomic injury which though definite was not sufficient to produce cystocele or rectocele, etc. This type of injury is termed "relaxation."

TABLE VIII

	WITH	WITHOUT
Anterior Wall:		
Relaxation	13.1%	16.6%
Small cystocele	7.7%	15.3%
Large cystocele	1.5%	8.5%
High cystocele	0.7%	0.0%
Totals	<u>23.0%</u>	<u>40.4%</u>

The immediate results of delivery without episiotomy showed the presence of anterior wall lacerations which did not occur in the episiotomy series. We consider the late results of anatomical analysis to support the opinion that the vagina must be considered as a tube, that despite its more adequate bony support, there is a large percentage of anterior wall injury, and that episiotomy reduces the amount of that

TABLE IX

	WITH	WITHOUT
Posterior Wall:		
Relaxation	7.7%	11.1%
Small rectocele	3.1%	12.5%
Large rectocele	2.3%	4.2%
High rectocele	0.7%	0.0%
Totals	13.8%	27.8%

These results are interpreted to mean two things. In episiotomy the extent of injury is more easily determined and the damage done is more readily repaired.

TABLE X

	WITH	WITHOUT
Outlet:		
Slight R.V.O.	7.7%	19.4%
Marked R.V.O.	6.9%	13.9%
Totals	14.6%	33.3%

The anatomic evidence of outlet injury follows the trend of the preceding studies. In analysis of the results from a chronologic standpoint, we found that as we learned to sweep deeper into the tissues on the crown suture the incidence of outlet failures decreased tremendously in the episiotomy and major laceration series. The large percentage of failures in the no episiotomy series were the groups listed as *No* and *first-degree* lacerations.

We have considered the gradation of lacerations made immediately after delivery in the group in which no episiotomy was done. In order to determine the actual amount of damage incurred at that time, we have subdivided the late results in the group without episiotomy into subgroups under the degree of laceration recorded at the examination immediately postpartum.

TABLE XI

None (27) cases		First degree (17 cases)	
A	70.4%	A	41.2%
B	25.9%	B	35.3%
C	3.7%	C	23.5%
Second degree (20 cases)			
A	45%		
B	45%		
C	10%		

Other subgroups were too small to be of value.

In scanning these statistics we agree with R. P. Kelly that, "There are some cases who deliver without episiotomy and without laceration, but when they come in six to eight weeks later they do not have the same perineum." This series emphasizes the importance of submucous lacerations and the difficulty of recognizing and correcting them at the time

of delivery. The subgroups are small and can be accepted only as indicating trends. However, it appears that where nature has provided an adequate episiotomy, i.e., a second-degree laceration, the results are better than when she provides an inadequate one.

The study of the effect of age on results brings out another interesting point.

TABLE XII. EFFECT OF AGE ON RESULTS

Up to 20	WITH	WITHOUT	25 to 30	WITH	WITHOUT
A	71.4%	56.0%	A	85.7%	33.3%
B	28.6%	40.0%	B	14.3%	44.5%
C	0.0%	4.0%	C	0.0%	22.2%
20 to 25	WITH	WITHOUT			
A	75.8%	57.1%			
B	22.7%	28.6%			
C	1.5%	14.3%			

In general all the groups with episiotomy show the same proportions. In each instance the comparison of later results is in favor of the episiotomy group. With each advance in age the group delivered without episiotomy shows a marked increase in the unsatisfactory results. We interpret this as evidence that the indication for episiotomy becomes stronger as a primipara passes the age of twenty, and that the indication is more mandatory with each successive year.

Inasmuch as 9.4 per cent of primiparas can be delivered without laceration and without demonstrable anatomic injury at follow-up, and inasmuch as an additional 19.8 per cent, though lacerated, show a Grade A result, we are not ready to join Gusman and Tritsch in their campaign for prophylactic episiotomy. We *are* ready, however, to paraphrase the old surgical dictum and say, "When in doubt, cut." Little has repeatedly called attention to the necessity for episiotomy in those patients with contracted bony outlets or narrow subpubic angles. DeLee has advocated it in preparation for rapid forceps deliveries, Pomeroy, as a precursor to version and the complex forceps rotations. We wish again to emphasize that this study is based on patients delivered under optimum hospital conditions. We do not advocate elective episiotomy except as a hospital procedure.

#### SUMMARY

Two hundred and two primiparas delivered at term by forceps are studied comparing the immediate and late results with and without episiotomy.



The types of episiotomy are considered, and it is suggested that the mediolateral type is the safer in the prevention of third-degree lacerations.

It is shown that, in our hands, much better anatomic results are obtained following episiotomy and repair. It is suggested that the better results are attributable to the easier recognition of the extent of injury done in episiotomy and the simplification of the repair where a surgical laceration is produced. It is shown that episiotomy spares the anterior wall. It is suggested that where the spontaneous laceration approaches adequate episiotomy the percentage of unsatisfactory results is less. The fallacies of examination in attempting to determine the exact amount of damage done immediately after delivery without episiotomy is shown. It is further suggested that the indication for episiotomy becomes mandatory in proportion as the age of the primipara exceeds twenty years. Many of the series are inconclusive because of the smallness of the subgroups. They are presented not as adequate studies but as indices of the trends and the need for additional investigation.

#### REFERENCES

- Anspach, Brooke M.*: Am. J. Obst. p. 1711, 1915. *Braun, Carl*: Lehrbuch, 1867 (quoted from Little). *Broomall, Anna*: Am. J. Obst. p. 517, 1878. *DeLee*: Principles and Practice of Obstetrics, Philadelphia, 1928, W. B. Saunders, p. 326-B. *Dührssen*: Arch. f. Gynäk. p. 27, 1890; p. 413, 1893 (quoted from DeLee). *Cameron*: American Textbook of Obstetrics, p. 877 (quoted from Lubin). *Gusman, H. A.*: Ohio State M. J. 28: 653, 1932. *Jewett*: American Textbook of Obstetrics, p. 373 (quoted from Lubin). *Kelly, R. P.*: Virginia Med. Monthly 57: 397, 1930. *Lubin, S.*: Long Island M. J. 60: 81, 1932. *Little, H. M.*: Curtis' Obstetrics and Gynecology 2: Philadelphia, 1933, W. B. Saunders Co., p. 366. *Michaelis*: See von Winekel's Handbuch 3: 1, p. 153 (quoted from Little). *Ould*: Treatise on Midwifery, p. 1742 (quoted from Little). *Plass*: AM. J. OBST. & GYNEO. 22: 176, 1931 (quoted from Watson). *Polak, J. O.*: Manual of Obstetrics, New York, 1914, D. Appleton-Century Co., p. 180. *Pomeroy, R. H.*: Trans. Am. Gynec. Assn. 43: 201, 1918. *Stahl*: Ann. Gynec. & Ped. p. 674, 1895. *Stander, H. J.*: Bull. Johns Hopkins Hosp. 47: 233, 1930 (quoted from Watson). *Tritsch, J. E.*: J. Am. Inst. Homeopathy 23: 327, 1930. *Von Ritgen*: Neue Ztschr. f. Geburtsh. 3: (quoted from Little). *Watson, Benj.*: Curtis' Obstetrics and Gynecology 11: Philadelphia, 1933, W. B. Saunders Co., p. 256. *Williams, J. W.*: Obstetrics, ed. 6, New York, 1930, D. Appleton-Century Co., p. 379.

## CURRENT TECHNIQS FOR OBSTETRIC ANALGESIA AND ANESTHESIA<sup>1</sup>

CHARIS GOULD, M.D., AND B. C. HIRST, M.D., PHILADELPHIA, PA.

(From the Post-Graduate Course in Gynecology and Obstetrics, Graduate Hospital)

THIS is an analysis of twenty-four answers to an inquiry sent out by Dr. B. C. Hirst regarding the technic for obstetric analgesia and anesthesia used in a number of clinics, distributed as follows: California 2, Canada 1, Connecticut 1, Illinois 2, Louisiana 1, Massachusetts 1, Michigan 1, Minnesota 2, Missouri 3, New Jersey 1, New York 6, Pennsylvania 1, and Wisconsin 2. In three of the clinics reporting the department of anesthesia of the hospitals cooperates in the administration of obstetric anesthetics. Two of the replies were from the departments of anesthesia of the respective hospitals.

### ANALGESIA

Information regarding analgesia was obtained from twenty-three sources, of which twenty-one have some "routine" or "standard" procedure which they follow. Flexibility of procedure and "individualization" of the treatment are stressed in three.

The time of administration varies little. In one clinic, medication is withheld until the cervix is 7 to 8 cm. dilated, but the analgesia is usually begun in primiparas as soon as the pains have become strong and regular, lasting one-half to three-quarters minutes, with five- to three-minute intervals, and the cervix dilated 3 to 5 cm. In multiparas the time of administration is determined by the character and frequency of the pains rather than by the condition of the cervix. The methods most commonly employed involve the use of barbiturates, morphine and scopolamine, and rectal ether, alone or in combination.

Barbiturates are used in sixteen clinics, and in three distinct ways:

1. As adjuvants to other types of hypnotics in 3 clinics
  - Sodium amytal, 2
  - Pentobarbital sodium, 2
2. As principal hypnotic in 12 clinics
  - Sodium amytal alone, 3 (in multiparas only, 1)
  - Sodium amytal with scopolamine, 1
  - "Barbiturates" (unspecified) with scopolamine, 1
  - Phenobarbital, 1
  - Pentobarbital sodium, 5
  - Pentobarbital sodium with scopolamine, 6

Pentobarbital sodium with morphine, 1

Numal, 1

Pernocton, 1

3. To prolong the action of morphine and scopolamine in 1 clinic  
Dial, 1

The apparent discrepancy in the above figures is explained by the fact that in several clinics more than one preparation is employed. Since in some of the papers "pentobarbital" is apparently used as a synonym for the sodium salt, while in others allusion is made simply to "the pentobarbitals," these have been grouped together under the appropriate headings with pentobarbital sodium in the tabulation.

Sodium amytal or pentobarbital sodium is used early in the first stage in nervous patients who later receive morphine and scopolamine after sufficient progress has been made. In one clinic pentobarbital sodium is used "in connection with the morphine and scopolamine," but no details are given.

The most frequently used of the barbiturates is pentobarbital sodium with or without scopolamine. The technique of Irving and his coworkers at Boston Lying-In Hospital as published in *Surgery, Gynecology and Obstetrics* for January, 1934, is used in three clinics and modifications of his procedure in four more. The modifications consist in variation of the initial dose of the barbiturate or of interval and dose of scopolamine. One clinic substitutes sodium amytal for the pentobarbital. Most clinics use rectal ether to control the restlessness induced by the barbiturate. In one clinic repeated small doses (1.5 to 3 gr.; 0.09 to 0.18 gm.) of pentobarbital sodium are used; a maximum of 6 gr. (0.36 gm.) usually is sufficient to carry the patient over to the second stage. In this clinic morphine is used in rare cases of primiparous labor "early in the first stage" before the pentobarbital sodium is given, and rectal ether is used afterward in primiparous labors, or those prolonged by errors of rotation.

In one clinic where a pentobarbital-scopolamine technique is sometimes followed, sodium amytal is occasionally substituted for the pentobarbital in the same dosage.

In general, a large initial dose of pentobarbital sodium, with or shortly followed by an injection of scopolamine which is repeated as necessary, seems to be preferred to frequently repeated small doses of the barbiturate. The usual dose is 4 to 6 gr. (0.24 to 0.36 gm.) but as much as 7.5 gr. (0.5 gm.) is given at the first dose. Excitement is less and recovery more prompt, requiring less nursing supervision. One clinic remarks that the drug can be used late in labor with greater safety than morphine.

Sodium amytal is not widely used. In one clinic it is used in multiparas in place of the morphine and scopolamine which is routine in primiparas. The usual dose is 5 gr. (0.3 gm.).

Four clinics simply listed the drugs used without giving dose or method of use.

In one clinic a 10 per cent solution of allylisopropyl barbituric acid, marketed under the name of Numal, is being used intravenously, in doses of 100 mg. per kilogram of body weight, injected at the rate of 1 c.c. per minute. In their hands it has given 90 per cent satisfactory results in a series of 231 cases without harmful effect to mother or child. The users are enthusiastic, but this is not reported from any other clinic under consideration. The product is used in France with reported success.

Pernocton is given intravenously in one clinic when morphine or gas has interfered with the uterine contractions in a patient who has had a prolonged first stage and is exhausted. The contractions are said to improve and a labor which had come to a definite standstill is said to advance rapidly.

The use of dial (diallyl barbituric acid) to prolong the effect of morphine and scopolamine is mentioned by one clinic, but their series is not complete, and they do not wish to make a definite statement at this time.

There are two types of combined analgesia involving barbiturates. One clinic uses morphine sulphate gr.  $\frac{1}{6}$  (0.01 gm.), scopolamine gr.  $\frac{1}{150}$  (0.0004 gm.), and sodium amytal gr. 6 (0.36 gm.) by mouth, followed after four to six hours with scopolamine gr.  $\frac{1}{200}$  (0.0003 gm.) subcutaneously, repeated once two or three hours later if necessary. The same technic is used in multiparas, using  $\frac{1}{4}$  gr. (0.0075 gm.) of morphine.

In another clinic the morphine, gr.  $\frac{1}{6}$  (0.01 gm.) is given by mouth with 3 gr. (0.18 gm.) of pentobarbital sodium, which is repeated without the morphine at four-hour intervals for two more doses.

Most clinics do not combine morphine with the barbiturates, and one specifically mentions the increased danger of respiratory depression, and also feels the use of barbiturates is contraindicated in cardiac patients because restlessness increases the strain on the heart.

One reports an increased incidence of fetal asphyxia with barbiturates, type and technic unspecified, which led to their being discontinued, but two definitely state that there was no fetal asphyxia observed. One other clinic has discarded barbiturates as "unsatisfactory"; another would have continued their use if adequate nursing facilities had been available.

Morphine and scopolamine are used in eight of the reporting clinics. The dose of morphine varies from  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (0.015 to 0.0075 gm.) and that of scopolamine from  $\frac{1}{100}$  to  $\frac{1}{200}$  gr. (0.0006 to 0.0003 gm.) for the initial dose. The scopolamine is usually repeated in smaller doses, and in one instance as little as  $\frac{1}{400}$  gr. (0.00015 gm.) is used. Two of

them report the use of morphine in smaller doses in slowly progressing multiparas, while in one, sodium amytal was substituted as has been mentioned. In three clinics the morphine is repeated if the labor is prolonged, but the usual practice is to repeat the scopolamine alone, and in one clinic the morphine is never repeated after the initial dose. Two clinics specify that they do not use morphine within four hours of the expected delivery, while one does not use it within six hours. The intervals for the repetition of scopolamine vary widely. The first dose of scopolamine is given from forty-five minutes to one and one-half hours after the initial dose of scopolamine with morphine. The interval seems to bear no relation to the size of the initial dose either of morphine or scopolamine. Scopolamine is repeated once, twice, or as necessary, although in one clinic "gas" is used after about 7 cm. dilatation of the cervix rather than repeat the scopolamine. Three clinics use heroin  $\frac{1}{12}$  to  $\frac{1}{25}$  gr. (0.005 to 0.0024 gm.), in one, heroin is used combined with scopolamine instead of morphine. One of these clinics states that if the heroin were not available, morphine and scopolamine would be used.

In two clinics dilaudid,  $\frac{1}{32}$  gr. (0.0018 gm.) has been used combined with the scopolamine instead of morphine with satisfactory results. The incidence of fetal asphyxia is in one clinic reported to be less than with morphine.

Three clinics occasionally use pantopon gr.  $\frac{1}{3}$  (0.02 gm.) with scopolamine. Results are satisfactory, but it is not routine.

Rectal ether alone is used in two clinics, in one for multiparas only. The Gwathmey technique is used in primiparas, modified by omission of the magnesium sulphate in one clinic, and of both the magnesium sulphate and quinine in another.

Avertin is still used "in selected cases" in one clinic and has been used and abandoned in two others.

Inhalation anesthesia is used during the first stage in five clinics, usually in multiparas, as follows: "gas," 1; ethylene and oxygen, 2; nitrous oxide and oxygen, 2. In one clinic nitrous oxide and oxygen is used throughout labor for private patients.

Of the 23 clinics reporting on analgesia 17 used one standard method, either barbiturates, morphine and scopolamine or a combination of both, 3 report the use of 2 methods, 2 of 3 methods, and 1 listed 5 different drugs "used in selected cases."

#### ANESTHESIA

Twenty-four clinics reported on anesthesia. One reports only on anesthesia used in operative obstetrics and has been reserved for separate consideration. An attempt to study the techniques of the remaining re-

ports dividing the anesthesia arbitrarily into four classes, 1 late second stage, 2 actual delivery, 3 repair, and 4 operative obstetrics gave the following results for 23 cases.

	LATE SECOND STAGE		DELIVERY	
	CASES	%	CASES	%
Inhalation anesthesia	22	95.7	21	91.3
Nitrous oxide and oxygen, with or without ether	15	65.2	12	52.1
Ethylene and oxygen	3	13.0	5	21.7
Ether	3	13.0	3	13.0
Chloroform	2	8.7	4	17.4
Infiltration	0	0.0	2	8.7

The percentage of those using nitrous oxide and oxygen may actually be higher than is here shown, but three clinics report the use of "gas" and are included only in the inhalation anesthesia. It is implied by some that repair is done under the anesthetic used during the late second stage and delivery, but insufficient detail makes comparable statistics for the proposed third and fourth classes impossible. In two which use gas in the late second stage and chloroform for delivery, ether is used during repair. Several clinics use either nitrous oxide and oxygen or ethylene. In one clinic chloroform is given throughout to patients unless contraindicated. In another chloroform is used when there is fetal distress to relieve the pressure on the child, followed with large amounts of oxygen alone, and no attempt is made to deliver the child until the fetal heart regains its normal rate. Indeed, the head of the child is sometimes pushed upward to relieve any tension on the cord while the chloroform is being given. It is also used in neglected cases with tonically contracted uteri.

Only nine clinics reported operative obstetric anesthesia separately.

One uses phenobarbital or pentobarbital sodium as preoperative sedative in 1.5 to 3 gr. (0.09 to 0.18 gm.) doses.

Three use local infiltration anesthesia, two for low forceps or repair only, one for laparotrachelotomy. In one of these, pudendal block is also used. The agents are not stated by one clinic, in the others novocaine or mepercaine are used, strength not given.

One uses spinal anesthesia in operative deliveries where there is no contraindication. It is not recommended for the termination of normal labor. Technique is not given.

Two prefer ether for caesars and ether is often used in versions and extractions, manual rotations, and where relaxation is insufficient with the use of gas alone. Ethylene and cyclopropane are sometimes used with nitrous oxide and oxygen anesthesia to obtain better relaxation.

Divinyl ether and cyclopropane are still in the experimental stage. The present cost is prohibitive, but results are said to be good.

In one clinic an elaborate technique for cesarean section starts with nitrous oxide and oxygen, adding ether two or three minutes before the

incision is made. As soon as the babe's mouth is freed, the anesthetic is stopped and carbon dioxide and oxygen is given until the cord is clamped. Then a hypodermic of morphine and atropine or of pantopon and atropine is given the mother, the oxygen in the nitrous oxide and oxygen mixture is reduced, and the operation terminated under this anesthetic, usually without ether.

It is possible that these data do not represent the whole trend of obstetric anesthesia and analgesia in this country, but they have been collected from widely divergent locations and from outstanding clinics and teaching centers. No attempt has been made to extend the scope of this paper by including a survey of recent literature. It is, however, interesting to note that in none of these centers is paraldehyde used. F. Neon Reynolds in his book, *Relief of Pain in Childbirth*, published in London in 1934, dismisses the barbiturates as dangerous, but advocates paraldehyde in oil per rectum, with or without a single injection of morphine and scopolamine, for "ease of administration, general applicability, effectiveness, and ready combination with other methods" (notably nitrous oxide and oxygen or chloroform) "during the expulsion stage." Rosenfield and Davidoff of Boston published in 1932 a series of 50 cases in which they used paraldehyde with sodium pentobarbital with no failures. In *Surgery, Gynecology and Obstetrics* for February, 1935, they present a series of 300 cases with 1/335 failures, and in these the distress incident to the labor was greatly decreased, but the desired amnesia was not obtained. There was no maternal mortality in either series, and no fetal mortality which could be attributed to the use of the drugs. Excitement occurred in 7.33 per cent of cases.

Colvin and Bartholomew of Atlanta, Georgia, report in the *Journal of the American Medical Association* for February 2, 1935, a series of 100 cases in which sodium amytal was used with rectal paraldehyde, with no increase in length of labor or of incidence of postpartum hemorrhage, no fetal asphyxia, and so little excitement or restlessness in the patients that the authors do not hesitate to suggest its use in the home, in spite of the fact that it is generally accepted that obstetric analgesia should be undertaken only in hospitals where adequate nursing facilities are available.

#### CONCLUSIONS

Statistical analyses of small groups are necessarily misleading, but we believe the following general conclusions are justified for the group under consideration:

1. There is a striking lack of unanimity of type and technic of obstetric analgesia and anesthesia.
2. The most widely used analgesic agents are the barbiturates, among which pentobarbital sodium appears the most frequently chosen.

3. The barbiturates are given by mouth; their intravenous use has not spread extensively in the United States.

4. Barbiturates are frequently combined with scopolamine or occasionally with morphine and scopolamine.

5. Excitement induced by the barbiturates is controlled by rectal ether.

6. In general, barbiturates are not considered to increase fetal asphyxia.

7. Barbiturates have not proved universally satisfactory and have been discontinued in some clinics.

8. Barbiturates require careful nursing care of the patient while under their influence.

9. Morphine with scopolamine is the second most common type of analgesia used.

10. It is believed to increase fetal asphyxia and is not used within four to six hours of expected delivery.

11. Avertin is not widely used.

12. The Gwathmey technic is occasionally used, and is usually modified by omission of either the magnesium sulphate, the quinine, or of both.

13. Inhalation anesthesia is rarely used during the first stage.

14. On the contrary, inhalation anesthesia is almost always used during the late second stage and during delivery.

15. Nitrous oxide and oxygen, alone or with ether, is the most widely used of the inhalation anesthetics.

16. Ether is used where relaxation is necessary, and is preferred for cardiac patients to other inhalation anesthetics.

17. The use of ethylene seems to be fairly well restricted to clinics located in the Middle West.

18. The place of spinal anesthesia in obstetrics is distinctly limited.

19. Local anesthesia is not widely used.

20. The ideal of obstetric analgesia and anesthesia has not yet been attained.



## EXTRAUTERINE PREGNANCY\*

### A CLINICAL STUDY OF 500 CASES

JAMES E. FITZGERALD, M.D., AND JOHN I. BREWER, M.D., CHICAGO, ILL.

(From the Departments of Obstetrics and Gynecology of Northwestern University Medical School, St. Luke's Hospital and Cook County Hospital)

THE diagnosis and treatment of extrauterine pregnancy have been the subject of much thoughtful study since they were first recognized as a clinical entity. In the past few years, an enormous amount of literature has appeared on this subject. Nevertheless, the diagnosis still presents great difficulties as is evidenced by the percentage of error, and the mortality tables convince one that the ability to diagnose such cases and the method of treating them deserve further investigation.

This group of 500 cases consists of 402 cases from Cook County Hospital and 98 cases from St. Luke's Hospital. All cases from Jan. 1, 1924, to the middle of 1934 are included, and they are consecutive except where a case history is unavailable. All of the cases were proved extrauterine pregnancies by operation, autopsy, or tissue study.

At the Cook County Hospital, extrauterine pregnancy is considered as pathologic obstetrics, and when such a diagnosis is made on admission, the patient is assigned to the obstetric service. Because of the obscurity of diagnosis, such patients not infrequently go to a medical or surgical service. About an equal number are admitted to each of the gynecologic and obstetric services. Almost as many are sent to the gynecologic service diagnosed as pelvic infections, as are sent to the obstetric service as extrauterine pregnancies. Thus, it happens that the cases here reported have been cared for by any member of the surgical staff, one of the six gynecologists, or one of the five obstetricians on the hospital service.

*Age.*—The extremes of age were sixteen and forty-nine years. More than three-fourths of the patients were between the ages of twenty and thirty-five. Extrauterine pregnancy, like many other diseased conditions, has been thought by various authors to be seasonal in occurrence. Our statistics covering a period of ten years fail to show any noteworthy variation in this respect.

*Previous Deliveries.*—We have not attempted to designate previous pregnancies because in this class of patients the history of previous abortions is notoriously inaccurate. There were 27.4 per cent of these women who had delivered no full-term babies; 18.2 per cent had delivered only one; 18.4 per cent had two babies. Thus, 64 per cent of the 500 had two babies or less. Thirteen patients were operated upon previously for tubal pregnancy.

*Time Elapsed Between Last Pregnancy and Ectopic Pregnancy.*—The time elapsing between the date of the last pregnancy and the development of the ectopic

\*Read before the Chicago Gynecological Society, January 18, 1935.

varied from six weeks after the birth of a full-term child to nineteen years, the average time being 4.7 years. In the cases where such information is available, a long period of sterility is not the rule, more than half of the extruterine pregnancies being recorded within three years after the birth of the last child.

*Bleeding.*—Menstrual disturbance is a common factor in the history of a patient who has an extrauterine pregnancy. The classic history of such a patient is rather generally accepted as that of a missed menstrual period followed at a later date by mild irregular bleeding usually characterized as spotting. In our series of cases, however, more than one-third did not miss a menstrual period, at least from a lay point of view. Nevertheless, the majority of these did show a menstrual disturbance. Thus, fifty-seven patients (11.4 per cent) had bleeding which began as a menstrual bleeding at the normal time, but continued longer than a normal period, and in sixty-four (12.8 per cent) the normal period was replaced by a diminished and intermittent flow described as spotting. In a slightly larger group the patient definitely missed a menstrual period, and began to bleed vaginally from four days to fourteen weeks after a menstrual period should have occurred. In eighty-eight cases (17.6 per cent) there was no bleeding at any time. Thirty of these developed symptoms before they had missed a menstrual period, and fifty-eight had a history of missed menstrual periods but no subsequent bleeding. One patient had not menstruated for two years, but she had a definite glandular dysfunction.

*Character of Bleeding.*—Eighty-eight of our patients (17.6 per cent) had no vaginal bleeding between the time of the last normal menstrual period and the time at which a diagnosis of some condition requiring operative interference was made. More than half of the total (50.6 per cent) had only spotting following normal menses and while a few (6.4 per cent) spotted only one day, the great majority spotted intermittently for various periods. In a fifth of the cases (20.6 per cent) moderate bleeding was noted, and in 8.2 per cent there was bleeding that could be characterized as profuse. Two patients had actual hemorrhage, and in these cases the external flow was apparently sufficient to account for the evident blood loss.

*Type of Pain.*—Pain of some type is an almost universal complaint of a patient with an extrauterine pregnancy. It was present in 96.4 per cent of our cases. Every adjective description of pain has been used by these patients. The striking feature, however, is the high percentage in which sudden, severe pain was noted. This occurred in nearly two-thirds of the entire group, and in more than half of all cases it was the first pain noted by the patient. Various characterizations of this type of pain are met with, but practically all patients were agreed upon one point, namely, that it was a sudden pain which was so severe as to force them to suspend their activities immediately. That this sudden, severe pain is not invariable is evidenced by the 34.8 per cent who never had pain of any severity. Ten patients had no pain at any time. Two of these cases were unruptured tubal pregnancies discovered while operating upon patients with fibroids. Advanced extrauterine pregnancy may be present in the absence of pain, as was shown by one ruptured interstitial pregnancy with a four months' intraabdominal fetus, and one patient with an extrauterine mass as large as a four months' pregnant uterus, neither patient having pain at any time.

Thus the localization of pain was not of great help in either the diagnosis of extra-uterine pregnancy or in determining its site. In our experience, shoulder pain was helpful more as corroborative evidence than as a primary diagnostic factor.

*Temperature.*—Forty patients (8 per cent) had a temperature below 97° F. These patients were all seriously ill and in collapse. There were 35.6 per cent who had normal temperature; 41 per cent showed only a mild elevation in temperature, that is, not over 100° F. Thus, 84.8 per cent had a temperature of 100° F. or below.

*Sedimentation.*—A sedimentation test was done in 19 instances. In 18 of these there were varying amounts of intraperitoneal bleeding. Seven tests were normally horizontal. Nine were single curves and 3 were diagonal. In none was there a rapid sedimentation.

*Admission Pulse.*—Of this group of 500, only 42 (8.4 per cent) had a pulse of 80 or below. Two hundred forty-five (49 per cent) had a pulse of 100 or above. Of these 119 were above 120.

*Leucocyte Count.*—A leucocyte count was recorded in 339 cases. In one-third of these it was within normal limits, and in two-thirds there was a definite increase. On the whole, this increase was mild, over one-third ranging between ten and fifteen thousand, while less than 14 per cent showed more than twenty thousand.

*Erythrocyte Count.*—The erythrocyte counts were all taken on admission of the patient to the hospital. The time at which these counts were made undoubtedly accounts for the fact that over 60 per cent of those patients on whom red cell counts were recorded showed a count of more than three million.

*Pelvic Findings.*—Several interesting facts are apparent in a study of the results of pelvic examination. Palpable masses were found in a large majority of the cases (65.2 per cent). Bleeding sufficient to cause bulging of the culdesac was noted in more than one-third (33.8 per cent). The frequency of extreme tenderness was striking. Tenderness characterized as either extreme or marked was noted in 71 per cent of our patients. This phenomenon has been subject to much dispute. Litzenberg<sup>1</sup> describes the pelvic mass of an ectopic as "tense, fluctuant, exquisitely tender and pulsating." He also observes that the cervix is excessively sensitive to movement when there is peritoneal irritation from blood in the culdesac. Anspach<sup>2</sup> says, "A prominent and often a striking feature of the palpation is the marked tenderness of the pregnant tube. It is not unusual for the patient to start with pain at the first touch of the examiner's finger." Schumann<sup>3</sup> says, "It is noteworthy that the tenderness on vaginal examination is usually out of all proportion to the size and density of the mass palpated, and to the experienced gynecologist the disproportionate tenderness is highly suggestive of the presence of an ectopic gestation, as against acute salpingitis. Traction on the cervix and active manipulation of the uterus greatly aggravates the pain and tenderness." Our experience has been that tenderness is almost invariably present when there is a palpable mass and that in the majority of cases the tenderness is extreme. In those cases where a mass is not palpated, excessive tenderness is frequently the factor which enables one to make the proper diagnosis. In the estimation of this factor it is to be remembered that the great majority of these patients were seen long after the onset of symptoms. Patients seen very early might show less tenderness. Thus Curtis<sup>4</sup> observes, "In the region of the affected fallopian tube is a boggy, usually non-sensitive, sausage-shaped or ill-defined mass." However, the majority of his patients were seen early.

*Preoperative Diagnosis.*—The preoperative diagnosis was correct in 60.4 per cent of the cases. It was, therefore, incorrect in nearly 40 per cent. The greatest difficulty in differential diagnosis was caused by the similarity of history, symptoms, and findings in extrauterine pregnancy and chronic inflammatory processes. Thus

51 patients (10.2 per cent) were operated upon under the diagnosis of inflammatory disease and 53 patients (10.6 per cent) as either ectopic or inflammatory disease. In addition to these, 23 patients (4.6 per cent) were operated upon with the indefinite diagnosis of surgical abdomen.

*Location of the Pregnancy.*—Tubal pregnancies were about equally divided between the two sides. The most common location was in the outer one-third of the tube, and the least common in the inner third. There were eight cornual pregnancies. One patient had a cornual pregnancy on one side, and a tubal pregnancy on the other, both of which had perforated. Seven tubal pregnancies had perforated into the broad ligament. There were fifteen secondary abdominal pregnancies, the youngest of which was three months and the oldest eight months, the average age being 4.6 months. In six patients, both tubal and intrauterine pregnancies were present. After operation three of the patients aborted and three carried the uterine pregnancy to term.

*Associated Pathology.*—Until fairly recently, previous pelvic infection has been considered the most important factor in the causation of extrauterine pregnancy. Many observers have also noted that evidence of previous infection was by no means universally present. In this group of 500, clinical evidence of resolving adnexal infection was definitely noted in 142 cases (28.4 per cent). It is to be expected that in a certain percentage evidence of previous pelvic infection was present but not recorded on the record of operation. The other cases in which associated pathology occurred requires no comment, except that in several of the cases of fibromyomata the ectopic pregnancy was the incidental finding, as it was in one case of incarcerated umbilical hernia.

*Patients in Collapse.*—Ninety-one of the 500 patients came to the hospital in collapse. They showed marked pallor and a rapid, thready, soft pulse, often imperceptible at the wrist. They had cold, moist extremities, often air hunger and usually a subnormal temperature. Frequently they were restless and often semiconscious. It is not the purpose of this report to discuss the physiology of this condition, nor to enter into the old argument of the merits of immediate versus delayed operation. Suffice it to say that immediate blood transfusion is almost an impossibility at the Cook County Hospital, because of the necessity of depending on relatives to act as donors.

Of these 91 patients, one-third died and two-thirds recovered. Strangely, the same percentage of each group was operated upon at once, and the same percentage had the operation delayed. In this group of 91 patients in extremely serious condition, the mortality of those operated upon at once was 34 per cent, and of those treated for shock before operation the mortality was 33 per cent. While there may be some room for argument as to the proper time to operate upon these patients, there can be no argument about the value of immediate blood transfusion in exsanguinated patients.

*Fainting, Nausea, and Vomiting.*—Fainting was noted in 145 patients. It was almost invariably preceded by a sudden attack of severe pain. In a large number of patients, both of these symptoms occurred in association with a desire to defecate. Nausea and vomiting was a symptom in 187 patients, or more than one-third of the group.

*The Unruptured Group.*—In 34 cases there was no apparent perforation of the tubal wall and no blood in the peritoneal cavity. For the purpose of this report, these were considered unruptured tubal pregnancies. In these cases the menstrual history and the character of bleeding was not unlike that of the other cases. The diagnosis was even less accurate because several of these were discovered in connection with other pelvic pathology which was correctly diagnosed.

The absence of sudden severe pain was noteworthy in the unruptured cases. In the 500 patients, sudden severe pain was present in about two-thirds of the patients, but in the unruptured cases cramps were the only pain complained of by two-thirds of the patients. In 2 cases there was no pain at any time.

*Mortality.*—A mortality of 7.8 per cent is rather higher than that of most series recently reported, and requires comment, if not explanation. There are two factors which have some bearing on this high mortality. One is that the Cook County Hospital is an emergency hospital which receives a fairly large percentage of patients who are already beyond help. The other is that there is no means of obtaining blood for transfusion except from relatives, and relatives of the patients in this hospital are notoriously unwilling to submit to this procedure.

Of the 23 postoperative deaths resulting from hemorrhage and reaction to operation, only 3 patients were transfused. Three patients with secondary abdominal pregnancy died. None was transfused. Experience over a period of years has taught us that exsanguinated patients are bad risks whether operated upon or not, and it is our opinion that a large percentage could be saved if prompt blood transfusions were available for them. The other postoperative deaths explain themselves. It is of interest to know that the patient who died from thrombosis had no evidence of pelvic infection or thrombosis at autopsy. The thrombosis occurred in the jugular and left subclavian veins, the superior vena cava and the right auricle.

Twelve patients died before operation. Ten of these were considered beyond hope of operative help, and all of them died a short time after entrance. Not one of these patients received a blood transfusion. Two patients who died before operation deserve comment. Both were in excellent condition on admission. In one a cul-de-sac puncture was done as a diagnostic procedure, and no blood was found. Although she was afebrile on entrance, a massive pelvic infection developed after the needling and a subsequent colpotomy revealed old blood and pus. The patient died from the infection. The other patient who was not operated upon was examined in the afternoon, at which time she had a pulse of 72, was afebrile and, except for the history, had no evidence of an extrauterine pregnancy. She was kept for further observation. At 11 o'clock the same night she had a sudden severe pain, collapsed, and died within an hour.

The average stay of all patients in the hospital after operation was 15.1 days, the extremes being nine and ninety days. The time of operation varied from twenty to ninety minutes, and the average time was forty-nine minutes.

#### SUMMARY

1. A series of 500 extrauterine pregnancies is presented.
2. A long period of sterility preceding the extrauterine pregnancy was not the rule in this group.
3. Pain of some type was the most common symptom. In two-thirds of the patients sudden, severe pain was noted.
4. In the majority of the unruptured cases the pain was of a cramping character.
5. Abnormal bleeding was present in a majority of the patients.

6. Approximately one-third of the patients had missed no menstrual period.
7. Severe collapse occurred in 18.2 per cent.
8. Fainting was noted in 29 per cent of the patients.
9. Over half of the patients had a temperature above normal.
10. Extreme pelvic tenderness was present in nearly three-fourths of the cases.
11. The mortality rate was 7.8 per cent.
12. Blood transfusion is the most important single factor in the treatment of cases in collapse.

## REFERENCES

(1) *Litzenberg, Jennings C.*: Nelson's Loose-Leaf Surgery 7: 523. (2) *Anspach, B. M.*: Curtis, Obstetrics and Gynecology 3: Philadelphia, 1933, W. B. Saunders Co., p. 402. (3) *Schumann, Edward A.*: Extrauterine Pregnancy, New York, D. Appleton and Company, p. 131. (4) *Curtis, Arthur H.*: Textbook of Gynecology, p. 342, and personal communication.

104 SOUTH MICHIGAN AVENUE

122 SOUTH MICHIGAN AVENUE

---

## A SERIES OF 627 VAGINAL HYSTERECTOMIES PERFORMED FOR BENIGN DISEASE WITH THREE DEATHS\*

N. SPROAT HEANEY, A.B., M.D., F.A.C.S., CHICAGO, ILL.

AT THE 1934 meeting of the American Gynecological Society I reported a series of 565 vaginal hysterectomies performed for the cure of benign disease with two deaths, a mortality rate of 0.35 per cent.<sup>1</sup> At this time I wish to report on an additional sixty-two cases or a total of 627 cases with three deaths or a mortality of 0.47 per cent. This includes all patients operated upon since the Staff at the Presbyterian Hospital adopted ethylene as the routine anesthetic in major surgical work. During this time no case requiring a vaginal hysterectomy was treated in any other way. As a matter of fact a great number of women were successfully operated upon by the vaginal route, on whom I formerly would have done an abdominal hysterectomy either because of the size of a tumor or from the fear of adhesions, or would have given radium because they would have been considered poor surgical risks. You will notice in the table, in spite of this being a report on benign disease, several patients with cancer. The preoperative diagnosis in these cases was nonmalignant disease and the operative findings did

uterus were so early as to eliminate infection from our consideration and those of the ovary carried no risks to immediate recovery. When the preoperative diagnosis is cancer of the uterus either of the body or of the cervix, a more radical procedure is indicated, and in addition, such cases are always infected, so that frank uterine cancers are eliminated from this report. This study is an attempt to evaluate the risks of an operation.

Thus far I have not had to abandon the vaginal route and complete the operation abdominally. Of the 627 cases 127 were nulliparas. Earlier I failed to keep a record of the number of cases requiring morecellation. It was performed thirty times in the last 168 cases.

TABLE I. AGE INCIDENCE

14 between ages of	25 to 29
200 between ages of	30 to 39
319 between ages of	40 to 49
70 between ages of	50 to 59
19 between ages of	60 to 69
5 between ages of	70 to 76

TABLE II. INDICATIONS

Fibromyoma of the uterus	338
Uncontrolled menorrhagia	119
Prolapsus of the uterus	76
Adenomyoma of the uterus	60
Persistent leucorrhea (uterine origin)	9
Sterilizing procedure	6
Retroversion	5
Uncontrollable dysmenorrhea	3
Prolapsus of the uterus with tubal pregnancy	1
Previous interposition operation producing bladder symptoms	1
Endometriosis of uterus and ovaries	1
Ovarian cyst and carcinoma of the cervix	1
Ovarian cyst	2
Dermoid cyst	1
Stricture of cervix	2
Bilateral chocolate cysts of ovary	1
Bladder tumor	1

One patient was operated upon for ovarian cyst and carcinoma of the cervix. The cervix did not appear malignant; it was badly scarred. The patient was very stout and advanced in years, and the uterus was removed in order to facilitate the removal of the ovarian cyst. Cancer was not suspected until the microscope was used. Likewise eleven other

TABLE III. COMPLICATIONS

Hypertension, systolic blood pressure over 150	79
Secondary anemia, hemoglobin under 60	71
Nephritis or albuminuria	22
Pulmonary tuberculosis (arrested)	5
Splenomegaly	1
Diabetes	5
Mitral stenosis	2

cases, unsuspected at operation, were microscopically cancer, four carcinomas of the cervix, four microscopic carcinomas of the corpus uteri, and three carcinomas of cervical polyps. There were two fibromyomas associated with carcinomas of the ovary.

TABLE IV. ADDITIONAL OPERATIVE PROCEDURES

Posterior colpoperineorrhaphy	303
One or both tubes removed	126
One or both ovaries removed	99
Plastic on urethra for incontinence	81
Removal of Bartholinian cyst	6
Removal of adenomyoma of rectovaginal septum	7
Repair of complete perineal tear	3
Repair of rectovaginal fistula	1
Repair of fistula in ano	1
Vulvectomy	1
Hemorrhoidectomy	2

TABLE V. COMPLICATIONS

Temperatures over 100.6° F. for one or more days	227
Due to cystitis	35
Probably due to wound infection	188
Femoral thrombophlebitis	1
Parotitis	1
Sponge in vaginal vault	1
Pulmonary embolus	1

The three fatal cases were as follows:

CASE 1.—Patient, operated upon for fibromyoma and menorrhagia, died on the fifth day of peritonitis. Microscopic examination showed the uterine wall to contain myriads of microscopic abscesses. It was later revealed that the patient had had an exploratory curettement within a week of her entrance upon my service and had kept this to herself.

CASE 2.—Patient had had a previous operation on appendages. During the hysterectomy the adherent ileum was incised but immediately sutured. Patient died on the fourth day from intestinal obstruction. An operation for the relief of the obstruction was performed but too late to be beneficial.



*Injury to the Rectum.*—Adenomyoma of the reetovaginal septum is not infrequently associated with disease of the uterus requiring a hysterectomy. This complication should not deter one from operating vaginally, for this growth is more amenable to attack by the vaginal route than it is abdominally. As a matter of fact I have frequently removed an adenomyoma of the reetovaginal septum and attended to the associated involvement of the ovaries by the vaginal route without removal of the uterus. When the uterus has to be removed, the procedure is greatly faecilitated. In this series seven required removal of adenomyomas of the reetovaginal septum. In one a tiny perforation of the rectum was made. Immediate suture in layers with interrupted catgut was followed by an uncomplicated convalescence.

*Prolapse of Fallopian Tube.*—In three eases, at some time during the convalescence, the vaginal vault opened and a tube prolapsed and became adherent in the vaginal vault. In such eases the patients usually complain of a profuse watery discharge. This accident is simply attended by making slight traction on the tube under anesthesia until it is completely delivered into the vagina, when a ligature is passed around the tubal mesentery and the tube burned off with a light nasal cautery. This generally requires no hospitalization. Previous to this series when closure of the vaginal vault was perfected with continuous suture tubal prolapse was not uncommon. These patients suffered no more inconvenience than would be occasioned by the removal of excessive granulation tissue.

In general the patient was able to eat breakfast and read the daily paper the morning after the operation. When extensive plastic work had also been done the disturbance experienced was that of the plastic work rather than that of the hysterectomy. When simple hysterectomy was done the patient was singularly devoid of complaint. None of the patients had shock. None had acute dilatation of the stomach. Except for the three fatal eases the attendants experienced only rarely anxiety regarding the condition of a patient. The average length of stay in the hospital in the 627 eases was 12.03 days.

There has never been reported a series of hysterectomies by the abdominal route with so low a mortality or morbidity rate. Vaginal hysterectomy should be more frequently performed. Every gynecologist should be able to perform safely this operation when the specific indications for it arise.

## VAGINAL APLASIA AND CREATION OF AN ARTIFICIAL VAGINA\*

S. LEON ISRAEL, A.B., M.D., PHILADELPHIA, PA.

*(From the Mount Sinai Hospital)*

THE following case history is worthy of record because two unusual congenital defects coexisted, vaginal aplasia and ectopic kidney. It is of further interest because a surgical "cure" was effected by the formation of an artificial vagina and by nephrectomy.

E. R., white, unmarried female, aged twenty-four years, was admitted to the Gynecologic Service of the Mount Sinai Hospital, Sept. 6, 1934, complaining of acute abdominal pain, nausea, and vomiting. The patient had never menstruated, but had suffered attacks of lower abdominal pains for three to four days at monthly intervals since the age of twelve. These periodic seizures had gradually increased in intensity and usually forced her to bed. Three weeks prior to admission, she experienced the accustomed episode of pain, but it was unduly persistent and accompanied by chills, fever, and vesical irritation. Hospitalization was occasioned by a sudden, tearing pain in the lower abdomen. The patient's family, social, and past medical histories were otherwise irrelevant.

On admission the patient was acutely ill. Her temperature, pulse and respiratory rates were 100° F., 100 and 20, respectively; blood pressure was 112/80. The abdomen was distended, markedly rigid and tender in both lower quadrants. Because there was no vaginal opening (Fig. 1), pelvic examination was performed rectally. The latter disclosed a pelvic mass the size of a grapefruit. All the secondary sex characteristics of a normal adult female were present. Aside from a moderate leucocytosis, laboratory studies (including serology) were normal.

were split, separating the two surfaces of each labium (Fig. 3). Two catgut sutures were drawn from the dome of the prepared space to the upper edges of the respective labial flaps. The flaps were inverted into the canal, raw surface to raw surface, and

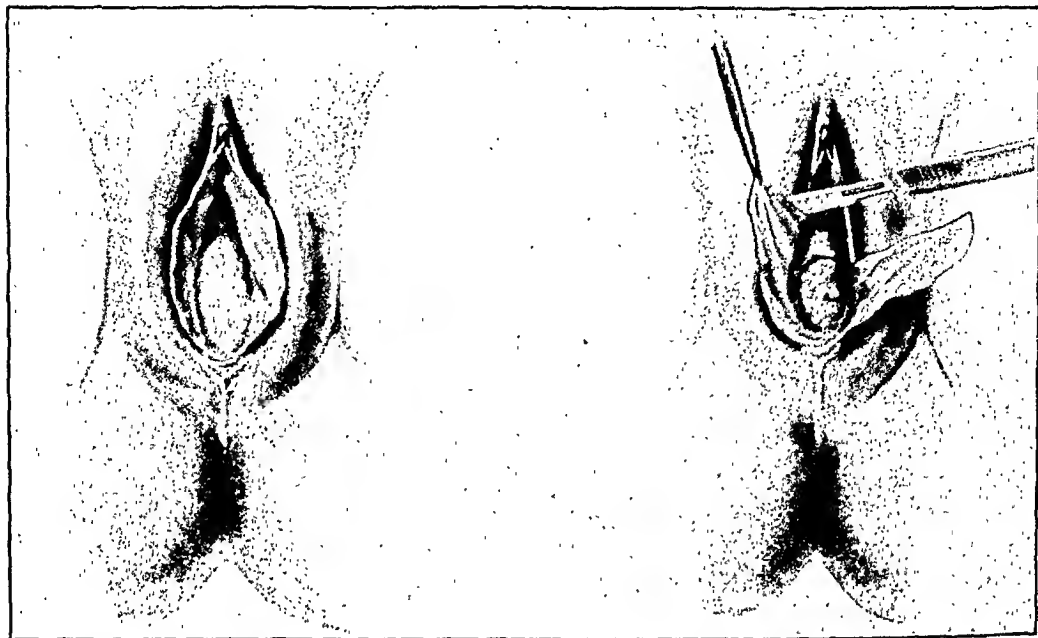


Fig. 1.

Fig. 2.

Fig. 1.—Vaginal aplasia. The labia minora are large and well suited for adaptation as flaps of a pedicle graft.

Fig. 2.—Artificial channel between bladder and rectum is packed with gauze. The labia minora dissected from above downward.

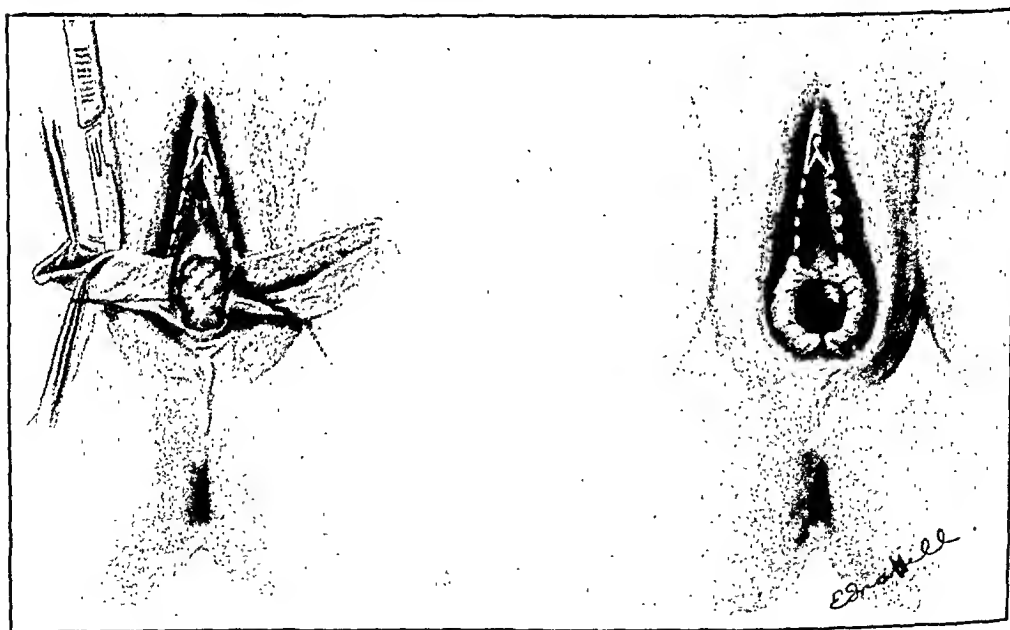


Fig. 3.

Fig. 4.

Fig. 3.—Labial flaps split and unfolded. Wound edges above sutured.

Fig. 4.—Labial flaps inverted into prepared canal and sutured to each other. New vagina lined by skin of labia minora.

the sutures tied. The grafts were united in situ to form a tube by several additional sutures (Fig. 4). Thus, the walls of the canal were the cutaneous surfaces of the

dissected labia minora. The new vagina was packed with vaseline gauze and an indwelling bladder catheter was inserted. Both packing and catheter were removed in forty-eight hours. Beginning on the eighth postoperative day, digital dilatation of the artificial vagina was instituted and performed daily for six weeks to combat excessive contraction of the grafted flaps. The vagina, five months after its formation, easily admits two fingers to a depth of  $2\frac{1}{2}$  inches.

The pyuria reappeared and was traced to the left kidney by cystoscopic examination. An excretory urogram disclosed a normal right kidney and ureter; the left kidney failed to excrete dye, necessitating a retrograde pyelography which showed the existence of a pyonephrotic, ectopic left kidney lying at the pelvic brim (Fig. 5). Partial drainage of the infected kidney was effected through a No. 12 indwelling ureteral catheter which remained in situ for many days periodically. No improve-



Fig. 5.—Pyelogram (retrograde) revealing left ectopic kidney. Note the markedly dilated calices.

and removed without undue blood loss. Convalescence from this third operation was uneventful. When discharged on Jan. 29, 1935, a month after the last operation, the patient was free from pyuria and in good physical condition.

#### COMMENT

The exact frequency of vaginal aplasia is not known. It is always congenital and often symptomless, being associated with uterine aplasia. Its symptoms (primary amenorrhea, pelvic tumor, and abdominal pain) arise in the presence of a normal uterus. If the retained menstrual blood reaches the peritoneal cavity, peritonitis may occur.<sup>1</sup> The treatment of vaginal aplasia, in the presence of a functioning uterus, requires an abdominal hysterectomy and subsequent formation of an artificial vagina. Occasionally, the uterine cavity may be joined to an artificially formed vagina.<sup>2</sup>

Collective reviews of operations designed to create an artificial vagina have been presented by Kroemer<sup>3</sup> and Pemberton.<sup>4</sup> All such plastic operations require a channel to be burrowed in the areolar tissue between bladder and rectum. They differ only in the technique by which the artificial channel is converted into a permanent vagina. To this end, continuous dilatation alone and free grafts of various tissues (autogenous and heterogeneous) have been employed with varied success. The most widely accepted operation, despite the high primary mortality, has been the intestinal (ileum or rectum) transplantation type (Baldwin<sup>5</sup> and Schubert<sup>6</sup>). Less dangerous are the procedures which fashion an artificial vagina by adapting pedicle grafts from the thighs and labia.<sup>7</sup> The use of pedicle grafts from the labia minora require well-developed external genitalia. When such is the case, the labial operation recommends itself because of its relative simplicity.

The association of genital and renal anomalies has a relatively high incidence. Recently, Hodgson<sup>8</sup> recorded the simultaneous occurrence of ectopic kidney and vaginal aplasia. Ectopic kidney is also a congenital anomaly. It usually lies obliquely across the left sacroiliac synchondrosis, and is characterized by an anterior (nonrotated) renal pelvis, an abnormal blood supply, and a short ureter. Thus, nephrectomy of such an organ, though often indicated, is fraught with technical hazards.

#### REFERENCES

- (1) Meyer, R.: *Ztschr. f. Geburtsh. u. Gynäk.* 34: 456, 1896. Brown, R. C., and Brews, A.: *J. Obst. & Gynaec. Brit. Emp.* 37: 233, 1930. (2) Ward, W. D.: *Surg. Gynec. Obst.* 21: 655, 1915. Wagner, G. A.: *Arch. f. Gynäk.* 120: 136, 1923. (3) Kroemer, P.: *Prakt. Ergebn. Geburtsh. u. Gynäk.* 5: 89, 1912. (4) Pemberton, F. A.: *AM. J. OBST. & GYNEC.* 10: 294, 1925. (5) Baldwin, J. F.: *AM. J. OBST. & GYNEC.* 56: 636, 1907. (6) Schubert, G.: *Zentralbl. f. Gynäk.* 35: 1017, 1911. (7) Graves, W. P.: *Surg. Clin. N. A.* 1: 611, 1921. Davis, C. H., and Cron, R. S.: *AM. J. OBST. & GYNEC.* 15: 196, 1928. Frank, R. T., and Geist, S. H.: *AM. J. OBST. & GYNEC.* 14: 712, 1927; *ibid.* 23: 256, 1932. Grad, H.: *Surg. Gynec. Obst.* 54: 200, 1932. (8) Hodgson, N.: *Brit. M. J.* 1: 822, 1933.

## CANCER OF CERVIX AND VAGINA IN A CASE OF COMPLETE PROCIDENTIA

LEO BRADY, M.D., F.A.C.S., BALTIMORE, MD.

(From the Department of Gynecology, the Johns Hopkins Hospital and University)

MOST gynecologists believe that malignancy rarely develops in the prolapsed uterus, but Emmert and Taussig<sup>12</sup> in a recent article conclude that it does so not infrequently. These two observers report a series of ten cases of complete prolapse, in four of which malignancy had developed, and they write: "From this one may infer that if biopsies were made of all the decubitus ulcers of prolapsed uteri more cases of cancer would probably be discovered."

A study of the literature on cancer of the cervix and on complete prolapse should be of help in determining whether or not these two conditions are often or only rarely encountered together. As far back as 1882, Fritsch,<sup>1</sup> in Billroth and Pithru's *Handbook of General and Special Surgery*, wrote that it is remarkable that the prolapsed uterus seems to be almost immune against cancer. J. Williams,<sup>2</sup> in the Harveian lecture for 1886, reported a single case of malignancy occurring in a seventy-seven-year-old woman with a prolapsed uterus. In 1893, Pomtow<sup>3</sup> was able to collect only twenty-nine such cases in the whole medical literature. Kuntz<sup>4</sup> in the following year added to the literature the report of one more patient suffering from these two conditions. Of special interest is the article by Bäcker,<sup>5</sup> published in 1897. This author found just one instance of malignancy of the cervix in a prolapsed uterus in an investigation carried out at Budapest on 11,000 women, 755 of whom had uterine carcinoma.

Schmidt,<sup>6</sup> in 1898, added three additional cases to those already reported, but from then on there were no further reports of malignancy occurring in the prolapsed uterus until 1926. In that year Macleod<sup>7</sup> had under his care two women with this condition, and in 1929, Kraul<sup>8</sup> reported the case of a sixty-year-old woman with a prolapse as large as two fists and a carcinoma of the cervix, the size of the palm of the hand. In 1930, Höglers<sup>9</sup> reported the largest number of women with both prolapse and carcinoma of the uterus that up to that time had been observed in any one clinic. He summarized the history of five such patients treated in the University Frauenklinik of Vienna and added two other cases seen in the Frauenklinik at Prague. Nevertheless, most of the articles published in later years have indicated even more strongly than the earlier ones that malignancy rarely develops in the prolapsed uterus.

patient was only thirty-three years of age when she developed a carcinoma in the prolapsed uterus. This author stated that Pomerey of Cleveland, in 350 cases of the cervix studied microscopically, saw only this one that had developed in a prolapsed uterus. Finally, we come to the article by Emmert and Taussig on "Cancer and Prolapse of the Uterus." This report differs from any other published on this subject. Not only is it remarkable that these authors have had the opportunity to observe such an unusually large number of cases of malignancy developing in the prolapsed uterus, but what is particularly astonishing is that they studied only ten cases of prolapsed uteri and found all their four cases of malignancy in this small series.

A rather striking example of malignancy developing in a prolapsed uterus recently came under my care and arousing my interest in this subject led me to investigate the records of the Johns Hopkins Hospital. In 1900, Dr. T. S. Cullen<sup>14</sup> published his book, *Cancer of the Uterus*, based on the study of 147 cases of carcinoma of the cervix, studied between the years of 1893 and 1899 in the laboratory of Gynecological Pathology in the Johns Hopkins Hospital. In this group of 147 cases of cervical malignancy there was not a single case in which the carcinoma had developed in a prolapsed uterus. Cullen, himself, in 1920, operated at the Church Home and Infirmary on a seventy-five-year-old woman with a complete prolapse. The biopsy taken from her cervix showed squamous-cell carcinoma. She lived ten years and died from a condition in no way associated with the cervical cancer. This is the only case that Cullen has seen of malignancy in a prolapsed uterus. In 1923, Martzloff<sup>15</sup> published a series of articles, based on the study of 387 cases of carcinoma of the uterus that had been admitted to the Johns Hopkins Hospital. This author does not record a single instance of a carcinoma occurring in a prolapsed uterus.

The type of operation performed for prolapsus uteri varies in different clinics. At the Johns Hopkins Hospital the "Watkins interposition" is the procedure of choice. Usually but not always a part of the cervix is removed in this operation. The amputation carried out in such cases is not a high one but usually consists of the removal of only the hypertrophied and elongated portion of the cervix. Such an operation would certainly be unsatisfactory when used as method of treatment for carcinoma of the cervix. In spite of all this, a follow-up study, which I<sup>16</sup> made on fifty-six patients on whom the interposition operation was performed, did not show a single patient who in later years died from carcinoma of the uterus. These statistics from the Johns Hopkins Hospital seem to confirm the opinion of those who believe that malignancy seldom develops in a prolapsed uterus.

A brief report of a case which was recently under my care follows:

M. S., aged sixty-five, came to the Diagnostic Clinic of the Johns Hopkins Hospital on October 10, 1934, complaining that "her womb came down." She stated that the condition had been present for fifteen years, although she had never let anybody know about it until a few weeks before she entered the hospital. There had been a leucorrheal discharge for many years and in the last six months this had become bloody. The patient had had fourteen pregnancies. The menopause had occurred twenty years previously. The rest of the patient's history had no bearing on her gynecologic condition. The general physical examination was essentially normal for a woman of her age. The heart and lungs showed no pathologic changes. Blood pressure 142/80. The urine was negative on both chemical and microscopic examinations.

The gynecologic examination showed a prolapse of the uterus, which measured from the external urethra to the tip of the prolapse 15 cm. and which had a circumference of 30 cm. The external os of the cervix had been replaced by a hard

indurated ulcer, measuring  $4 \times 3$  cm. and on the left lateral vaginal wall there was a second ulcerated lesion, measuring  $6 \times 5$  cm. The latter did not connect directly with the other. Fig. 1 shows the appearance of these two ulcerated lesions and their relation to each other. Biopsies taken from the two lesions showed, microscopically, definite squamous-cell carcinoma. Because of the marked prolapse an operation was advised instead of radiation.

Dr. Elmer G. Hall, the patient's physician, referred her to me after she had been studied in the Diagnostic Clinic and asked me to operate on her at St. Joseph's Hospital. A vaginal panhysterectomy was performed with an extensive resection of the vaginal walls, so as to remove the carcinoma with as wide a margin as possible. Four-fifths of the entire vagina was removed with the uterus. In carrying out this



FIG. 1.—Aspect of cervix and vagina in a case of complete prolapse.



## SUMMARY

A case is reported of carcinoma developing in the vagina and cervix of a patient with a complete uterine prolapse. Studies made of the material in the Gynecological Pathological Laboratory show that this is the only case of its kind that has been seen in the Johns Hopkins Hospital.

Why the cervix of the prolapsed uterus should possess so large a degree of immunity to malignant degeneration has never been satisfactorily explained. One would naturally suppose that the converse would be true, for the cervix of the prolapsed uterus is constantly exposed to irritation and often is the seat of a chronic infection—factors that have been shown usually to predispose to the development of cancer. It has been suggested that the cornification of the cervical epithelium which develops in a case of complete procidentia protects the cervix against malignant degeneration. This may be a factor in protecting the prolapsed uterus, but it hardly seems sufficient to explain fully such marked resistance to the development of cancer.

Thanks are due Miss H. M. Carpenter for the accurate and expressive illustration.

## REFERENCES

- (1) *Fritsch, H.*: Die Lageveränderungen der Gebärmutter. Billroth und Pitha. Handbuch der allgemeinen und speciellen Chirurgie, Bd. IV. Abth. A, Abschn. IX, 1880. (2) *Williams, J.*: Cancer of the Uterus. The Harveian Lectures for 1886, London, 1888, p. 19. (3) *Pomtow, G.*: Carcinoma Uteri Prolapsi, Inaug. Diss., Berlin, 1893. (4) *Kurtz, W.*: Ueber Carcinom am prolabierten Uterus, Inaug. Diss., Tübingen, 1894. (5) *Bäcker, J.*: Arch. Gynäk. 53: 47, 1897. (6) *Schmidt, W.*: Monatschr. f. Geburtsh. u. Gynäk. 7: 506, 1898. (7) *Macleod, N. A.*: Brit. M. J. 2: 12, 1926. (8) *Kraul, L.*: Zentralbl. f. Gynäk. 53: 2104, 1929. (9) *Högler, H.*: Arch. Gynäk. 150: 135, 1932. (10) *Delvaux*: Bruxelles-Méd. 12: 325, 1931. (11) *Heidler*: Zentralbl. f. Gynäk. 57: 2941, 1933. (12) *Boukalik, W. F.*: AM. J. OBST. & GYNEC. 27: 620, 1934. (13) *Emmert, F. V., and Taussig, J. B.*: AM. J. OBST. & GYNEC. 28: 521, 1934. (14) *Cullen, T. S.*: Cancer of the Uterus, New York, 1900, D. Appleton and Co. (15) *Martzfloff, K. H.*: Bull. Johns Hopkins Hosp. 34: 141, 184, 1923. (16) *Brady, L.*: Surg. Gynec. Obst. 43: 476, 1926.

## MEDICAL ARTS BUILDING

Schilling, W.: Permanent Results of the Schauta-Stoeckel Vaginal Radical Operation for Carcinoma of the Cervix, Zentralbl. f. Gynäk. 57: 114, 1933.

The author reports statistics on 150 women seen in the Frauenklinik of Leipzig with carcinoma of the cervix who were treated by combined radical vaginal operation and roentgen irradiation. All diagnoses were confirmed by histologic section. The per cent of five-year cures, according to Winter's classification of extent of the disease at the time of admission, was:

GROUP	NUMBER OF WOMEN	NUMBER WELL AFTER FIVE YEARS	PER CENT
I	90	61	67.7%
II	34	18	52.9%
III	26	8	30.7%
	150	87	58.0%

Seven women received radium; 5 pre- and 2 postoperatively. In general, the women received 95 to 110 per cent of an erythema dose of roentgen rays through each of 6 ports, postoperatively.

The primary operative mortality was 6, or 4.0 per cent.

WILLIAM F. MENGERT.

## PREGNANCY IN A PATIENT WITH COMPLETE DOUBLE UTERUS

BRADFORD GREEN, M.D., AND C. KENNETH MILLER, M.D.,  
PHILADELPHIA, PA.

*(From the Greatheart Obstetrical Service, Temple University Hospital)*

GROSS anomalies of the genital tract are so rarely met that they prove perplexing to the obstetrician when pregnancy occurs. The present report describes the case of a young woman with a complete double uterus who has just passed through her first pregnancy with delivery of a normal healthy child.

Mrs. S. H. S., aged twenty years, was first seen by the authors in a gynecological clinic in April, 1932, with chief complaint of severe dysmenorrhea.

Menses began at eleven years; the patient had had marked dysmenorrhea starting three days before each period and lasting until three days after the period was over. In 1929, when fifteen years old, she had several attacks of acute abdominal pain, usually starting on one side and crossing to the opposite side. There was no vomiting; the attacks lasted for about twenty-four hours and disappeared. There was, however, during this time an almost constant dull pain in the right side, which frequently became sharp when rising from a sitting position. After an acute attack in July of this year, the patient was sent to the hospital and an appendectomy and right oophorectomy were performed.

The pathologic laboratory report states that the appendix was enlarged, with obliterated lumen, densely fibrotic walls, atrophied muscle and obliterated glands. The right ovary consisted mainly of a large luteal cyst filled with hyaloid material; the cyst walls and cortex were thin and sclerotic.

A diagnosis of obliterative appendicitis and luteal cystic ovary was made and the patient was discharged on the seventeenth day in good general condition. The family was informed at this time that the girl's genital organs were abnormal.

In 1932, the patient came to the gynecological clinic for treatment of the dysmenorrhea which for the past three or four months had become increasingly severe and necessitated remaining in bed for several days of each month. The pain started just above the symphysis and radiated chiefly to the left side, left loin, and down the left leg.

The patient had a normal menses on March 9, 1934, missed the next period, and soon experienced moderate nausea and frequency of urination. About ten days after the April period was due, there were slight cramps and spotting for two days, and at the time for each later period she had cramps and bleeding with clots of varying size. The duration and amount of flow were always less than normal.

Early in September the patient returned to Philadelphia and examination revealed both cervixes to be soft and closed but instead of being side by side as before, one was found to be directly anterior to the other. The uterus was globular, turned to the left, and extended to the level of the umbilicus. Fetal movements could be felt. On palpation no irregularity of the uterus or mass in the right adnexa could be discovered. One week later when a period would normally have been expected, the patient experienced severe crampy pains and expelled two pieces of tissue or blood clot the size of a hen's egg. These were lost, but definite shreds of endometrial tissue were expelled with bleeding for the next two days. No untoward effects on the pregnancy could be noted.

The clinical history led to the conclusion that the patient had a complete double uterus, that the pregnancy was in the left side, and that the menstrual bleeding was coming from the right. This symptom-complex was repeated four weeks and again eight weeks later with uterine contractions of sufficient severity to require bed rest for several days and repeated doses of morphia to prevent premature birth of the child.

At consultation it was decided that premature labor was almost sure to occur in view of the preceding history, that cervical dystocia with a long hard labor could be expected, and that rupture of the uterus must be guarded against. An elective cesarean section, as soon as the fetus was unquestionably viable, was believed to be the procedure of choice from the standpoint of both mother and child.

The patient was admitted to the Greatheart Service of Temple University Hospital at the end of the thirty-sixth week of pregnancy. She had been having irregular mild labor pains for two to three hours a day for the past week. Twenty-four hours after admission a midclassical cesarean section was done and a living female child was delivered, weighing 4 pounds 15½ ounces.

As soon as the uterus was closed and had contracted, it was thoroughly examined and found to have but one round ligament and one tube and ovary. A mass, the size of a goose egg, firm and regular, was palpated in the pelvis. When this was brought into view it proved to be the right uterus minus round ligament, tube and ovary. The right broad ligament with numerous adhesions was present. There were no bands or adhesions joining the two uteri.

The patient had poor vaginal drainage and a temperature ranging from 100° to 101° for seventy-two hours postoperative, followed by an uncomplicated convalescence. She was discharged from the hospital on the eleventh postoperative day with the abdominal wound completely healed, but with a moderate degree of subinvolution of the uterus.

The baby was kept in the hospital until four weeks old because of early weight loss and inability to maintain body temperature when not in an incubator. At two months she weighed 7 pounds 10 ounces and appeared to be thriving normally.

Examination of the mother eight weeks postpartum showed both cervixes small, firm, closed, and situated side by side. The left uterus was completely involuted, was in midposition, and the fundus bore over to the left. The right uterus could be barely palpated in deep midposition pointing to the right.

Pregnancy in double uterus is not unusual, but the carrying of such a pregnancy to a successful termination is rare.

An interesting factor in the present case is the establishment of menstrual periods, which were apparently normal for this particular individual, in the nonpregnant uterus as soon as the inhibiting effect of the newly formed corpus luteum became lessened.

Fortunately for the patient, the removal of the right tube and ovary makes it impossible for pregnancy to occur except in the left side. Otherwise she might have become pregnant in either uterus or become pregnant in one uterus when a pregnancy had already been established in the other, thus giving rise to all manner of complications.

The authors wish to acknowledge with thanks the courtesies and aid of Professor J. O. Arnold in the management of the case.

2021 WEST GIRARD AVENUE

---

## BILATERAL PERIPHERAL PARALYSIS OF THE RADIAL NERVE IN A NEWBORN INFANT

L. HOWARD SMITH, M.D., PORTLAND, OREGON

(From the Department of Pediatrics of the University of Oregon Medical School)

PARALYSIS of the musculospiral nerve (*N. radialis*) occurring in the newborn is of sufficient rarity to warrant recording. When I reported two cases of this unusual type of obstetric paralysis in 1916, only a few cases were mentioned in the literature. Since that time several have been reported. Kehrer<sup>2</sup> in his excellent monograph on paralysis of the arm in the newborn, collected some twenty eight reports of peripheral radial paralysis of the newborn. Langen's<sup>3</sup> article on radial paralysis in the newborn, in which he reports three cases of his own, is most complete.

I have been able to find only three cases of *bilateral* paralysis of the musculospiral nerve in the literature. One was reported by Koster<sup>1</sup> following fracture of both humeri. Kehrer<sup>2</sup> and Ottow<sup>2</sup> reported one case each where both radial nerves were paralyzed with resulting bilateral wrist drop.

For the next week he received calcium gluconate, 1 gm. with his feedings three times daily. Seven days after birth the blood showed calcium 9.4 mg. per 100 c.c. of serum and phosphorus 6.4 mg.

At this time the baby showed no twitching of the arms, color good, and nursing normally, but there was bilateral wrist drop. The deltoid biceps and triceps were used normally, and when the wrists and fingers were extended, the infant voluntarily contracted the flexors of the wrist and fingers, but no movement of the extensors



Fig. 1.—Showing bilateral wrist drop due to paralysis of both right and left radial nerves.

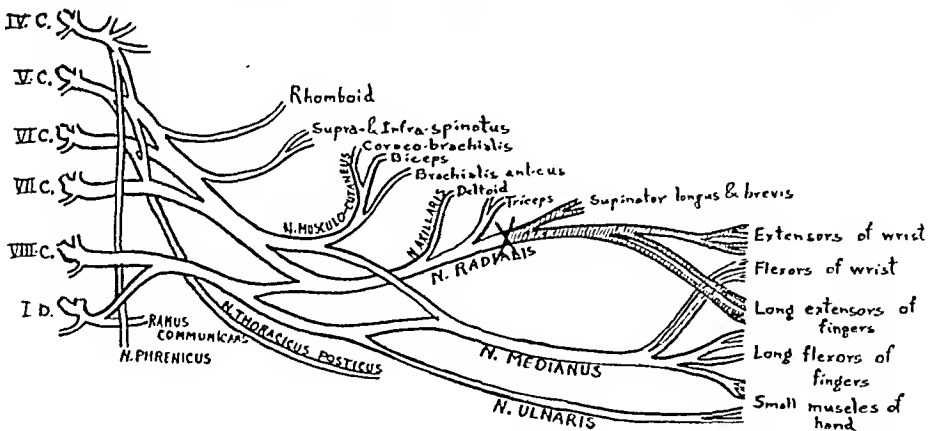


Fig. 2.—Diagram of brachial plexus. X. The probable site of injury to the *N. radialis*, distal to the muscular branches to the triceps but proximal to the branches given to the extensors of the wrist.

of the wrist could be elicited. Both forearms were placed in splints to prevent stretching of the extensor muscles. At the age of two weeks there was slight movement of extension of the fingers but not of the wrist. The blood calcium taken at this time showed 11.2 mg. and the phosphorus 6.2 mg. per 100 c.c. of serum.

When one month old wrists were extended voluntarily but muscular power was weak.

At no time was there any mark noted on the skin of the arm as the result of pressure, and x-ray examination of the bones of the arms was negative for fracture.

## COMMENT

Although there was some suggestive evidence of tetany of the newborn in this case, I do not believe it sufficient to warrant such a diagnosis.

The presence of Chvostek's facialis phenomenon in the newborn, as pointed out by Stevenson, Mitchell and Koch,<sup>6</sup> cannot be regarded as a pathognomonic symptom of tetany in the newborn. Jerking and twitching movements of the arms were present but there were no convulsions. The position of the hands simulating carpal spasm was doubtless due to contracting of the flexors of the wrists and fingers without the normal opposing extensors which were paralyzed. There was no pedal spasm. The blood calcium of 8.9 mg. per 100 c.c. of serum is below the average normal, but not as low as the expected calcium in tetany (6 to 7 mg. per 100 c.c.). However, cases presenting clinical symptoms of tetany in the newborn have been observed without marked lowering of the calcium (Shannon,<sup>7</sup> and Bass and Karelitz<sup>8</sup>). Rothstein<sup>9</sup> states that the diagnosis of tetany in the newborn will be suggested clinically by the presence of some or all of the following signs and symptoms: "Vomiting, hyperpyrexia, convulsions, twitches, tremors, carpopedal spasm, laryngospasm, positive Chvostek and Trousseau phenomena, and subcutaneous edema. Before intelligent treatment can be given, the diagnosis must be proved by the presence of a lowered blood calcium content."

Perhaps the case here reported is one of latent tetany, but regardless of the presence or absence of tetany, the infant showed definite paralysis of the wrist extensors with bilateral wrist drop.

The cause of the bilateral radial nerve paralysis with resulting wrist drop in the present case is rather obscure. Although no pressure marks were observed over the course of the radial nerve in the upper arm, the prolonged labor in a young primipara, with slightly less than the average normal pelvic measurements and the presence of an amniotic fluid thick with meconium, would indicate excessive pressure on the fetus during its passage through the birth canal. The presence of a pressure mark on the skin is not necessary in making a diagnosis of peripheral facial nerve paralysis when one observes paralysis of the facial muscles in a newborn.

The point of injury of the radial nerves in the present case (see chart) must be distal to the muscular branches to the triceps, but proximal to the branches given off to the supinator and extensor muscles of the wrists. This calculated point of injury is situated on the outer surface of the arm just above the external condyle where the radial nerve curves around the humerus.

## SUMMARY

A case of bilateral peripheral radial nerve paralysis in the newborn is reported.

The injury occurred distal to the branches of the nerve to the triceps, resulting in a bilateral wrist drop.

Several features suggestive of tetany of the newborn were present but insufficient to make a diagnosis of this condition.

The early use of splints to prevent stretching of the paralyzed muscles was an important element of treatment in restoring early function and in the prevention of permanent disability.

## REFERENCES

- (1) Smith, L. Howard: *Am. J. Dis. Child.* 2: 333, 1916. (2) Kehler, Erwin: *Ztschr. f. Geburtsh. u. Gynäk.* 108: 3, 1934. (3) Langen, Paulheinz: *Arch. f. Gynäk.* 139: 560, 1930. (4) Koster: *Deutsch. Arch. klin. Med.*, 1887. (5) Ottow, B.: *Zentralbl. f. Gynäk.* 56: 2714, 1932. (6) Stevenson, Mitchell and Koch: *Am. J. Dis. Child.* 34: 424, 1927. (7) Shannon, W. Ray: *Am. J. Dis. Child.* 48: 517, 1934. (8) Bass and Karelitz: *J. A. M. A.* 97: 1372, 1931. (9) Rothstein, Jacob L.: *J. Pediat.* 5: 341, 1934.

# OVARIAN PREGNANCY\*

## REPORT OF A CASE

HOWARD J. HOLLOWAY, M.D., EVANSTON, ILL.

MRS. B., aged twenty-six, consulted me to see if she was in sufficiently good physical condition to have another child. She had one child, aged five, and had had two spontaneous miscarriages at approximately twelve to sixteen weeks, respectively, with a history of fever and infection, following the last one, confining her to bed for several weeks.

Menstruation at fourteen, regular twenty-eight days, five-day duration, moderate flow, pains, cramps and backache first and second day. Uterus third degree retroversion, freely movable, normal size and consistency. Nothing abnormal felt in region of either adnexa. Cervix lacerated and eroded.

Patient was advised to have a tubal insufflation, which was positive, and cauterization of the cervix.

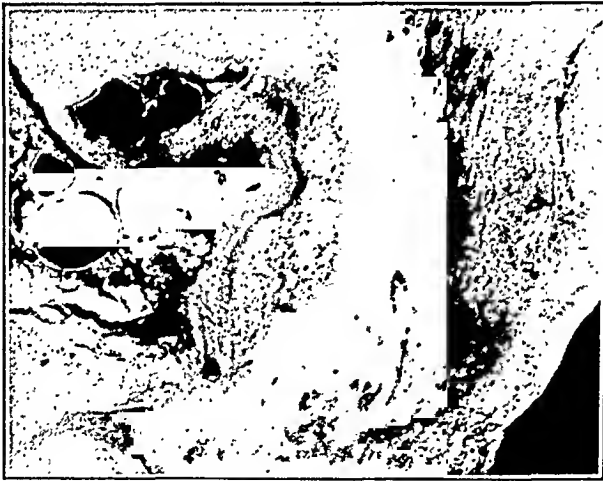


Fig. 1.

About six months later patient returned having gone over her expected date of menstruation about nine or ten days, complaining of being tired all of the time, sore breasts, some nausea and dizziness. On pelvic examination the uterus was only slightly, if at all enlarged, still retroverted but movable. Patient was given usual prenatal instructions. Five days later she called, stating that she had started slight bleeding. She was immediately put to bed, given sedatives, but continued bleeding. Two days following, patient passed a small piece of material which grossly looked like decidua. Fluid extract of ergot was then given, with tentative diagnosis of incomplete abortion. The tissue was examined microscopically and no chorionic villi could be seen.

Patient continued bleeding slightly and was advised to go to the hospital. The diagnosis then was of incomplete abortion or extrauterine pregnancy. This was five days since onset of bleeding.

\*Presented before the Chicago Gynecological Society, January 18, 1935.

At no time did patient have any pain until on entering the hospital when she started to have slight cramps in the right lower quadrant. Bimanual examination at this time revealed a swelling in region of right adnexa and about the size of a golf ball. The ovary could not be isolated separately from this mass. Dr. Heaney was asked to see the case in consultation, and the findings were verified, and a diagnosis of probable extrauterine pregnancy was made. Operation was advised. An Aschheim-Zondek test was not made. At this time patient had a temperature of 99°, red blood count 4,750,000, hemoglobin 87 per cent, white blood count 13,700, and urine negative.

This was exactly seven weeks since onset of last regular menstrual period, and six days since onset of bleeding.

The uterine cavity was examined and not enough material was obtained to explain the continued bleeding. The posterior culdesac was then opened and a small amount of dark blood was found in the peritoneal cavity. Both tubes were then examined throughout and found absolutely normal. Some fresh bleeding, however, could be seen coming from the right side, and on examining farther the right ovary was found to be bleeding and it was brought down into view in the culdesac incision. It was about the size of a large plum, half of which was a dark bluish red color and bleeding. This discolored portion with some normal ovarian tissue was resected and the remaining portion of the ovary closed with interrupted catgut. The culdesac was then closed in the usual manner.

The patient made an uneventful recovery, going home on the tenth day. Microscopic section showed normal ovarian tissue and chorionic villi.

---

## HUMAN OVUM IN A SALPINGITIS ISTHMICA NODOSA\*

A. F. LASH, PH.D., M.D., CHICAGO, ILL.

(From the Department of Gynecology of the Mt. Sinai Hospital and the University of Illinois, College of Medicine)

THE report of this section of a salpingitis isthmica nodosa is presented to demonstrate the often-mentioned cause of ectopic pregnancy.

This specimen was obtained from a twenty-eight-year-old nulliparous white woman. Her last period was from Sept. 15 to 18, 1934. The previous period occurred on August 19 to 23.

She was operated upon Sept. 22, 1934, because of severe persisting backaches due to a fixed retroverted uterus. At operation a typically healed (probably gonorrheal) pelvic peritonitis with cobweb adhesions was found fixing the corpus in the posterior culdesac. After freeing the corpus and adnexa, a right salpingitis isthmica nodosa was found and a right cystic ovary. The right tube was removed; the right ovary resected; the fimbriated end of the left tube was freed of adhesions, opened and insufflated; and the round ligaments were shortened. The patient made an uneventful recovery.

When she was seen on November 30, she related that her menses recurred on October 25 to 29 and on November 22 to 26. A tubal insufflation was performed and the left tube was found open.

The photomicrograph of the fallopian tube illustrates an ovum in a follicle of the isthmica nodosa which condition has been given so often as a cause of ectopic pregnancy. As to the age of the ovum one is unable to say definitely because of

---

\*Presented before the Chicago Gynecological Society, January 18, 1935.



the shrinkage and its degenerative condition. It is assumed it came from the ovulating follicle preceding the last menses. It appears degenerative with probable polar bodies. Serial sections could not be obtained because the pathologist of the hospital, Dr. I. Davidson, who recognized the ovum in his routine examination of the tissue, immediately had more sections made from the block but was unsuccessful in finding any further evidence of parts of the ovum.

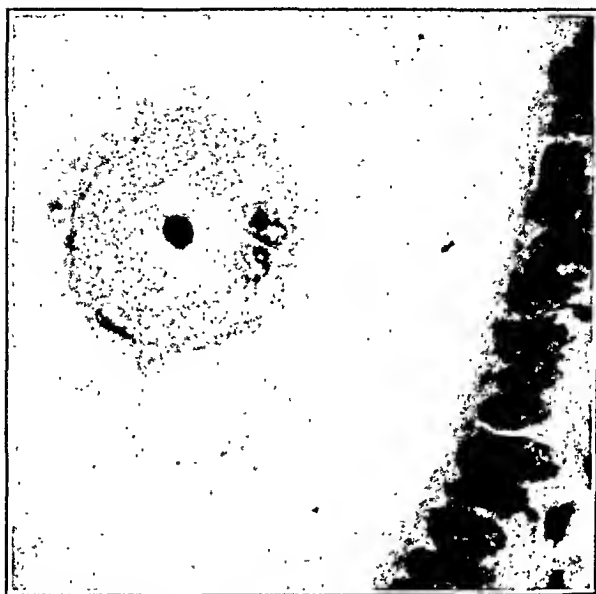


Fig. 1.—Human ovum in follicle of salpingitis isthmica nodosa. Ovum measured 31 microns.

Human tubal ova have been obtained by irrigating the tubes with normal saline and catching the washings in watch glasses for examination. Allen, Pratt, Newell and Bland studied nine such specimens, five of which proved to be ova. According to their investigations the size of the ova found in the tube shortly after ovulation varied from 90 to 180 microns. Paten and Gassmann have reported two human tubal ova.

30 NORTH MICHIGAN AVENUE

---

Vignes, Rodolfo E.: Carcinoma of Tube Presentation of a Case, *Bol. Soc. de obst. y ginec.* 13: 426, 1934.

After a discussion of the pathology and incidence of tubal carcinoma, which they find to be 0.4 per cent to 0.11 per cent of all genital carcinomas, the authors report a case. The treatment consisted in extirpation and postoperative x-ray irradiation.

MARIO A. CASTALLO.

# MYOFIBROMA OF THE OVARY WITH HETEROPLASTIC BONE FORMATION\*

IRVING F. STEIN, M.D., CHICAGO, ILL.

*(From the Michael Reese Hospital)*

THE tumor was taken from a patient sixty-six years of age, who was told some years ago that she had fibroids of the uterus, but who on account of her age declined any operative treatment. When I saw her, she stated that she sought relief



Fig. 1.



Fig. 2.

because pain had developed. She had, in addition, a huge cystocele. I could make out that the atrophic uterus was pushed to the right by a very large tumor which occupied the left side of the pelvis and extended to the level of the umbilicus. It was

---

\*Presented at a meeting of the Chicago Gynecological Society, February 15, 1935.

somewhat tender only in the lower portion. I diagnosed an ovarian tumor rather than an uterine fibroid, and that the symptoms were due to torsion. Operation under local and scopolamine and morphine, a midline incision was made just big enough to lift the tumor out of the abdomen. It arose from the right ovary but occupied the left side of the pelvis and abdomen, and had twisted 180 degrees on its pedicle. It was solid and extremely heavy, measured 18 by 11.2 by 9.8 cm., and weighed 1,400 gm. It was easy to untwist the pedicle, clamp and cut it, and remove the tumor. The patient made an uneventful and rapid recovery. The chief interest rested in the tumor itself, for it was very heavy and solid. Microscopic section showed a myofibroma with some bone formation (Figs. 1 and 2).

---

## CHRONIC TYPHOID ABSCESS OF THE OVARY

### REPORT OF A CASE

LOUIS A. SOLOFF, M.D., AND CLINTON S. HERMANN, M.D.,  
PHILADELPHIA, PA.

*(From the Pathological and Surgical Departments of the St. Joseph's Hospital)*

THE complications of typhoid fever are manifold and most of them are well known. Ovarian abscess, however, is so rare that it is not even alluded to in the textbooks of gynecology and medicine. About thirty cases are on record, three of which are American. It is an interesting coincidence that the last American case we found was likewise reported from the St. Joseph's Hospital of Philadelphia by F. Hurst Maier in 1914.

Miss N. O., aged 44 years, was admitted on Dec. 14, 1934, to the St. Joseph's Hospital with the complaint of severe sharp pain in the lower half of the abdomen. The pain began suddenly at 9:00 P.M. of the previous evening and was relieved partly by a soap-suds enema. This was followed by soreness in the right lower half of the abdomen. Upon examination, acute tenderness and spasticity were found in the right lower quadrant, and immediate operation was advised. The preoperative diagnosis was acute appendicitis. The blood count revealed a slight leucocytosis with a mild Schilling shift to the left. Erythrocytes, 4,550,000; leucocytes, 11,800; hemoglobin, 11 gm. per 100 c.c. (Haden-Hauser). *Differential Count*: Neutrophilic polymorphonuclear leucocytes, 77 per cent (27 band forms); lymphocytes, 15 per cent; monocytes, 8 per cent.

There was nothing significant in the past history except for an attack of typhoid fever in September, 1928, more than six years previous.

At operation, the right ovary was occupied by a cyst 6.5 by 6 by 5.0 cm. It was encapsulated by a glistening, translucent membrane beneath which there was soft gray yellow tissue averaging 0.4 cm. in thickness. In one region there was a small oval golden yellow flat piece of tissue resembling corpus luteum. Beneath the soft tissue there was a calcified shell 0.6 cm. thick which had to be opened with a saw. The cyst was filled with a foul creamy green yellow purulent material. Microscopically, the soft tissue proved to be ovarian tissue. The pathologic diagnosis was chronic typhoid abscess of the ovary with calcification.

Direct smear of the purulent material showed gram-negative bacilli. Hanging drop revealed them motile. It was then that typhoid was first suspected and the organism was studied culturally completely, including glucose, lactose, and blood agar, Russell's, Endo's media, litmus milk and gelatin. Those studied verified the im-

pression of a typhoid infection. A Widal was done on the patient's blood and found to be positive in 1:800 dilution. The organisms were tested with typhoid immune serum and found to agglutinate in 1:800 dilution. Finally, the patient's serum was tested against the organisms themselves and found to agglutinate them in 1:1600 dilution. Two months later, the patient's Widal was still positive in a 1:400 dilution. No organisms were found in the urine or feces.

#### DISCUSSION

Maier gives Walsberg and Kummel credit for reporting, in 1888 and 1890, respectively, the first cases of suppuration of an ovarian cyst following attacks of typhoid fever. Werth, in 1893, however, was the first to demonstrate the organism bacteriologically and Wallgren, in 1879, the first to apply the Widal test. Then followed case reports at irregular intervals, a complete list of which is appended in the references.



Fig. 1.—Chronic typhoid ovarian abscess showing peripheral calcification.

There are four possible routes by which typhoid fever may reach the ovary. (1) By ascending infection from the genital tract. (2) By direct extension from neighboring infected organs such as the intestinal tract. (3) By lymphatic spread. (4) Through the blood stream.

V. Oettingen reports an interesting case apparently illustrating the first avenue of infection. During a typhoid epidemic, a physician, immediately after examining a patient stricken with typhoid, did a vaginal examination on a woman who had recently aborted. The woman became sick and developed a long-continued fever. A growing ovarian cyst was palpable on bimanual examination. The Widal was strongly positive but no organisms could be isolated from blood, urine, or feces. Upon operation, typical typhoid bacilli were found in the ovarian cyst. The possibility and probability of ascending infection in this case cannot be denied.

Most cases of typhoid abscess of the ovary occur in dermoid cysts. The few remaining have occurred in pseudomucinous cystadenomas. Ours alone, we believe, has occurred in a previously normal ovary. The greater preponderance of dermoid

cysts has been attributed by V. Oettingen to adhesions to the intestinal tract and consequent direct or lymphatic spread. Maier, on the other hand, believes the typhoid bacillus shows a greater affinity for bone as evidenced by typhoid periostitis of the spine.

In all cases of typhoid infection of the ovary, a previous history of typhoid fever has been obtained. Inasmuch as typhoid fever in its earliest stages is always a septicemia, the hematogenous route is always at least theoretically possible.

Where there are no adhesions and no infection of the fallopian tube, as in our case, the hematogenous route is the only one possible. Perhaps circulatory disturbances, such as the kinking or twisting of a cyst with consequent temporary blockage of efferent vessels, passive congestion, and rupture of bacilli containing blood vessels, may explain the comparative frequency in cystic ovaries and the absence of circulatory disturbances in the normal ovary explains the comparative rarity in the latter.

The viability of the typhoid bacillus is notorious. Bland-Sutton reports a case of ovarian abscess with living bacilli sixteen years after the initial infection and our case represents more than five years. Usually, however, the ovarian complication is discovered one to eight months after the general infection or even during the course of the disease. It must be remembered, however, that typhoid abscess of the cyst or twisting of the pedicle may be the cause of its discovery. As stated previously, this may be the explanation for the apparent rarity in the normal ovary.

This study illustrates the value of bacteriologic examinations of obscure ovarian cysts.

#### REFERENCES

- (1) *Walsberg*: Berlin. klin. Wehnschr. p. 1008, 178. (2) *Kummel*: Centralbl. f. Gynäk. p. 81, 1890. (3) *Werth*: Deutsche med. Wehnschr. No. 21, p. 489, 1893. (4) *Sudeck*: München. med. Wehnschr. No. 20, p. 498, 1896. (5) *Pitha*: Centralbl. f. Gynäk. No. 37, p. 1109, 1897. (6) *Wallgren*: Arch. f. Gynäk. XIX, p. 15, 1899. (7) *Engelmann*: Centralbl. f. Gynäk. No. 23, p. 633, 1901. (8) *Lewis and Le Conte*: Am. J. M. Sc. 124: 590, 1902. (9) *Koch*: Monatsch. f. Geburtsh. u. Gynäk. 16: 198, 1902. (10) *Widal and Ravant*: Bull. et mém. Soc. med. d. hôp. de Paris, p. 45, 1902. (11) *Schipperowitch*: Frommel's Beiträge, 1904. (12) *Zatschenko*: Monatschr. f. Geburtsh. u. Gynäk. 19: 67. (13) *Dermoisier*: Centralbl. f. Gynäk. 28: 1171, 1904. (14) *Vignard*: Gaz. med. de Nantes 23: 641, 1905. (15) *Malldaigne*: Centralbl. f. Bakteriöl. 38: 249, 1905. (16) *Bensis*: Orient Med. February and March, 1906. (17) *Gaus*: Monatschr. f. Gynäk. 28: 163, 1908. (18) *Krinski*: Khirurg. Arkh. Velyaminora 27: 962, 1911. (19) *Winseh*: Jahrb. Geburtsh. 1911. (20) *Bland*: 1914. (22) *Wiener*: Jahrb. Gynäk. 1915. (23) *Abadie, J.*: Bull. et mém. evd. Nat. de chei, 1928. (24) *Laporte*: Bull. Bernardheig & Gumbazane, Bull. et mém. Soc. med. d. hôp. de Paris, p. 53, 1176, 1929. (25) *Papie, Morel, Lyon and Bertravel*: Bull. et mém. soc. med. d. hôp. de Paris 4: 1143, 1929. (26) *Brandao*: Bol. De. Coll. Brasil de Cir. 3: 30, 1932. (27) *Segal and Divoreeki*: Gynäk. Dolska 12: 675, 1933. (28) *Berger*: Lijecuvyes 55: 264, 1933. (29) *Van Heukohn*: Quoted by V. Oettingen. (30) *Mangold*: Quoted by V. Oettingen.

## ABDOMINAL PREGNANCY, WITH DELIVERY OF A LIVING CHILD

A. CHARLES POSNER, M.D., F.A.C.S., NEW YORK, N. Y.

*(From the Obstetrical Service of the Harlem Hospital)*

**B** P., COLORED, aged thirty, had given birth to two living children; one, weighing eight pounds, had been delivered normally in 1920, the other, weighing seven pounds, by forceps in 1922. A third pregnancy had been terminated at about three months. The family and personal histories were of no significance, except for an umbilical herniorrhaphy performed on the patient in 1931 at another hospital. Menstruation, which had begun at thirteen, had been regular every twenty-eight days until May, 1933, when "spotting" occurred; this was the last menstrual period.

In June, 1933, a diagnosis was made of uterine fibroids and a possible pregnancy, although the position and movements of the fetus could not be determined. The blood Wassermann reaction was four-plus, and antisyphilitic therapy was instituted. A roentgenogram taken June 9 revealed a five months' fetus displaced to the left, with evidence of a large mass in front and to the right. The Aschheim-Zondek test, performed June 12, was negative. The blood pressure was 128/80, the urine normal, and no signs of toxemia were present.

Late in August the patient came to the Antenatal Clinic complaining of a painful mass in the vagina, accompanied by a white, serous vaginal discharge. Minor complaints were of edema of the legs, headache, urinary frequency, dysuria, and terminal hematuria. She was told that the mass consisted of bulging membranes, and advised to return when in labor.

At 11:30 A.M., September 10, the patient presented herself for admission. Labor pains had begun at three o'clock that morning, at twenty-minute intervals.

Physical examination revealed an adult colored female having strong labor pains every ten minutes. Fever and chills were present, also. Abdominal examination showed a probable vertex presentation, with dorsum to the right. The fetal heart rate, in the left lower quadrant, was 140 beats per minute. Rectal examination was unsatisfactory. The cervix was entirely prolapsed; dilatation, one finger. The patient's tongue and lips were dry, the pharynx injected, the heart sounds of poor quality, the lower extremities edematous, and the reflexes hyperactive. The temperature was 100.2° F., pulse rate, 124; respiration, 32; blood pressure, 142/90. Blood culture and urinalysis were negative. The white blood count was 10,600; polymorphonuclear leucocytes, 68 per cent; transitional leucocytes, 3 per cent; lymphocytes, 29 per cent; red blood corpuscles, 3,800,000; hemoglobin, 60 per cent. Blood sedimentation time was 18 mm. in twenty-five minutes, 24 mm. in thirty-five minutes.

When the patient was examined again at two o'clock, she was dyspneic and ashen, and appeared older than her thirty years. The fetus seemed to be of about eight months' development, and presenting by the breech; no membranes or presenting part could be felt, however. The fetal heart rate was 160, in the left upper quadrant. In the culdesac was a large, hard, irregular mass, presumably a fibroid. The cervix, which was hypertrophic and edematous, was protruding from the vagina (Fig. 1). The anterior lip was eroded, and there was a left lateral laceration. A slight sanguinous discharge was present. The external os admitted two fingers.

After consultation laparotomy was decided upon because it was believed that delivery would be impossible otherwise and because abdominal pregnancy was suspected. The patient was prepared and sent to the operating room at 4:10 P.M. The abdomen was opened by a right paramedian incision under ether anesthesia. The uterus, about the size of a three months' pregnancy, was exposed. The rest of the abdominal cavity was occupied by a large sac filled with fluid and containing a fetus with its head to the left and feet to the right. The sac was brought to the anterior abdominal wall and opened. A living male child weighing seven pounds, thirteen and a half ounces, was delivered.

The patient's pulse became rapid, and immediate infusion was begun. The abdominal wound was closed in layers, and two Penrose drains with iodoform gauze were inserted into the sac. Preparation was made for transfusion. The patient went into shock in a few minutes and was revived by artificial respiration, carbon dioxide, adrenalin, and eoramine. Relapse occurred, however, and death ensued at 6:50 P.M.



Fig. 1.—Patient in labor, showing completely prolapsed cervix.

At postmortem examination performed the following day, a bacterial endocarditis, hitherto unsuspected, was found, and also fatty degeneration of the aorta and coronary arteries. Septic emboli and infarcts were seen in the spleen, liver, and kidneys. The gallbladder contained inspissated bile and several large cholesterol stones; the bile ducts were patent. The stomach was distended with gas. Scattered throughout the peritoneal cavity and attached to the mesentery were small, apparently encapsulated masses which on section were of a dark brown color and of firm consistency; these masses were found to be blood clots. The placenta and membranous sac were implanted primarily on the left ovary and secondarily on the mesentery, loops of the small intestines, and left broad ligament. The uterus extended from two and one-half to three fingerbreadths above the symphysis pubis. It was of fair consistency and contained several intramural fibroids. One fibroid about the size of an orange was situated on the lower part of the posterior wall; there was also a small polyp on the posterior wall. The right tube and ovary were macroscopically normal. Histologic examination of the left ovary through the site of implantation revealed chorionic villi and syncytial cells. The section through

the isthmal portion of the tube showed a decidual reaction, but no chorionic villi. Implantation of decidual cells was evident in a section of the small intestine.

Aside from the rarity of abdominal pregnancy at term with live delivery, this case is of interest because of the negative Asehheim-Zondek test, because of the completely prolapsed cervix, and because of the death of the mother from shock due to the effect of the sudden release of pressure on a heart already weakened by unsuspected bacterial endocarditis.

1132 PARK AVENUE

---

## INVERSION OF THE UTERUS IN TWO SUCCESSIVE PREGNANCIES\*

PAUL C. FOX, M.D., OAK PARK, ILL.

THIS case was seen in consultation at the West Suburban Hospital, Feb. 19, 1935, at which time the following history was given. The patient, aged thirty-five, para ii, had just delivered a seven-pound boy normally. She had been in labor sixteen hours and forty minutes. As far as she knew her first confinement had also been normal. Her past history was entirely negative.

About thirty minutes after the delivery, the physician in charge used a moderate amount of Credè expression. He soon noticed a bulging at the vulva which he thought might be the head of a second child, but very soon the entire uterus with the placenta attached to the fundus extruded through the vagina. There was profuse hemorrhage and marked shock. The attendant immediately removed the placenta from the fundus and attempted to reduce the uterus. While reducing the uterus he felt what he thought was a pedunculated fibroid, but which later proved to be the partially inverted fundus. He then packed the uterus thoroughly and called for consultation. When first seen the patient was in profound shock and it was impossible to do anything further at the time except to treat the shock. She was given morphine, glucose solution intravenously, and later a blood transfusion. None of these measures were of any avail. The patient made a brief rally, but soon relapsed and died about six hours after the inversion had occurred.

In looking up the history of this patient's first confinement it was discovered that at that time (September, 1931) she was under the care of another physician, and following a normal confinement, and a normal amount of Credè, she had an inversion of the uterus which was immediately corrected and from which the patient made an uneventful recovery. The attending doctor at this first confinement did not report this accident to the patient nor to any one else because he felt that he might be criticized, and since the patient recovered he simply left well enough alone.

This case illustrates the fact that inversion of the uterus can occur in properly managed cases and that it is not necessarily the fault of the attending physician. I am personally acquainted with both of the men who took care of this patient, and after careful inquiry I am convinced that no undue amount of force was used in attempting to deliver the placenta at either confinement.

715 LAKE STREET

---

\*Presented before the Chicago Gynecological Society, March 15, 1935.



## LIPOMA OF THE BROAD LIGAMENT\*

A. E. KANTER, M.D., CHICAGO, ILL.

A WOMAN, thirty-seven years of age, came to the hospital because of vaginal bleeding which had been present from September 17 to February 27, with the definite story that she had gone a number of days beyond her period. She had chills and fever, following which she had a severe hemorrhage. She consulted her physician who made a diagnosis of incomplete abortion and gave her something to relieve the pain. She had had four children, the youngest six years old.

Vaginal examination revealed the uterus very small and pushed over to the side. On the left side was a tumor mass rather soft, and reaching the crest of the ilium. With the story of chills, fever and a possible incomplete abortion, it was my belief that she had a hydrosalpinx on one side. On that diagnosis I opened the abdomen. The uterus was perfectly normal as were both tubes and ovaries. There was a tumor about the size of a large grapefruit situated in the broad ligament, pushing the sigmoid away. I opened up the broad ligament and easily enucleated a large lipoma with practically no bleeding. I closed the broad ligament and the patient made an uneventful recovery.

---

## FETUS PAPYRACEOUS IN TWIN PREGNANCY

### REPORT OF A CASE

JOSEPH G. CROTTY, M.D., CINCINNATI, OHIO

*(From the Obstetrical Service of the Good Samaritan Hospital)*

BOERLEIN, in 1931, reported a case of twin feti papyracei occurring in a triplet pregnancy, the third infant being delivered normally and at full term. He was able to find nineteen other cases in the literature including those of E. L. Moss (1921) and C. C. Wallin (1923). There are more frequent reports of single fetus papyraceous occurring in twin pregnancy, the other fetus being delivered at term. J. L. Mills reported such a case in 1923, and there are several other similar reports in American and foreign literature.

Mrs. B., a well-developed and well-nourished white gravida ii, twenty-six years of age, was admitted to the Obstetrical Service of the Good Samaritan Hospital (Cincinnati) on July 28, 1932, in active labor. Her previous pregnancy had terminated in a full-term stillborn infant, cause not known. Her last menstrual period began Oct. 20, 1931, and the present pregnancy had been entirely uneventful. Blood pressure and urine were normal and the Wassermann test was negative. Abdominal examination revealed a full-term pregnancy, O.L.A., fetal heart tones 140 in lower left quadrant. The cervix was well effaced, dilated about 4 or 5 cm., membranes were intact, the head was not quite engaged, and a hard, nodular mass presented at the internal os outside the intact membranes.

One hour later reexamination revealed the cervix completely dilated, the membranes still intact, the head engaged, and the hard, nodular mass now closely applied to the anterior vaginal wall.

One-half hour later the membranes ruptured and a full-term, living male infant was delivered spontaneously, simultaneously with a papyraceous fetus.

The papyraceous fetus was completely mummified, 1 cm. in thickness, and 14 cm. in length, and tallied quite closely with the descriptions and illustrations given in

---

\*Presented at a meeting of the Chicago Gynecological Society, March 15, 1935.

textbooks. The umbilical cord extended as a thin fibrous cord to a crescentic, white, hard, fibrosed placenta, continuous with that of the normal infant. Each fetus was surrounded by a separate amniotic and chorionic sac, but the sac with the papyraceous fetus contained no fluid.

3440 EDWARDS ROAD

## A MODIFIED VAGINAL SPECULUM

WILLIAM D. FULLERTON, M.D., F.A.C.S., CLEVELAND, OHIO

WHEN local applications are made to the vaginal walls in the treatment of inflammatory conditions, particularly such as caused by the *Trichomonas vaginalis*, it is very important that every portion of the affected mucosa be well exposed and easily accessible for topical applications.

The great majority of vaginal speculums in use today have a relatively broad anterior and posterior blade, which when in use, cover a very considerable portion of the vaginal mucosa and interfere with satisfactory exposure. To turn or twist these speculums after they have been introduced into the canal is mechanically difficult and often causes much discomfort to the patient.

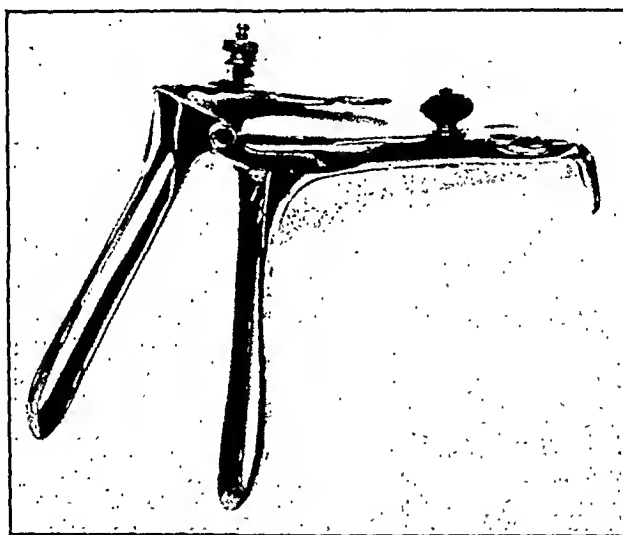


Fig. 1.

By a simple modification of the popular Graves' speculum this material objection is very satisfactorily eliminated. Both the anterior and posterior blades of the Graves' instrument have had their central portion cut out, leaving a fenestra, or window, the remaining skeleton edges of the blades are less than one-half cm. wide (Fig. 1). The instrument is made in three sizes, large, medium and small.

This modified instrument has clinically proved most satisfactory. Exposure of the vaginal walls is much more complete, and yet there is no material prolapse of the wall through the fenestra to obstruct the field of vision or to interfere with an excellent exposure of the cervix. Very rarely is even the slightest rotation of the speculum necessary to expose satisfactorily every portion of the vaginal mucosa at the same time.

NOTE: The instrument is made by the J. F. Hartz Company of Detroit, Michigan.

1508 KEITH BUILDING

# Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

## CESAREAN SECTION STATISTICS IN CHICAGO HOSPITALS

THE Maternal Welfare Committee of The Chicago Gynecological Society has been making a study for the past year of all types of deliveries in Chicago hospitals. This report gives the results of the cesarean sections.

The appended table shows that the percentage of cesarean sections in the small hospitals is 6.81. As the number of deliveries per year increases, the percentage of cesarean sections decreases until a percentage of 1.63 is reached for a hospital delivering between 900 and 1,000 mothers a year. Thereafter the percentage increases to 2.98 in hospitals delivering 1,500 or more per year. For comparison two dispensary services are shown in the table.

There were 37 deaths reported in 1934 following cesarean section. Since 1,800 hospital deliveries have not been reported to this Committee and, assuming that the percentage is carried through, Chicago should have had approximately 1,000 cesarean sections in 1934. This would give a death rate of 3.7.

The number of patients who died following classical cesarean section bears a ratio almost two to one over the low cervical cesarean section.

### CESAREAN SECTION DELIVERIES FOR 1934

Number of deliveries	-50	51-100	101-200	201-300	301-400
Number of hospitals	12	7	15	7	9
Number of deliveries	264	548	2,266	1,970	3,184
Low cervical	2	13	36	29	39
Classical	15	16	51	30	56
Porro	1	1			5
Vaginal		1	4	1	
Percentage cesarean sections	6.81	5.65	4.01	3.04	3.14
Number of deliveries	401-500	501-600	601-700	701-800	901-1,000
Number of hospitals	8	2	4	2	2
Number of deliveries	3,506	1,065	2,571	1,505	1,893
Low cervical	46	4	15	13	2
Classical	90	17	48	12	31
Porro	5	1	1	2	
Vaginal					
Percentage cesarean sections	4.00	2.06	2.13	1.78	1.63
Number of deliveries	1,001-1,100	1,500-plus	Dispensary	Grand	Total
Number of hospitals	3	3	2		76
Number of deliveries	3,132	9,012	2,422		33,338
Low cervical	53	210	8		470
Classical	28	39			433
Porro	1	20	3		40
Vaginal		2			8
Percentage cesarean sections	2.62	2.98	0.41		3.09+

Edward L. Cornell, M.D., Secretary.

# Society Transactions

---

## PHILADELPHIA OBSTETRICAL SOCIETY

*MEETING OF JANUARY 3, 1935*

*(See also page 151, July issue.)*

The following papers were presented:

**Hormonic Induction of Menstruation in Amenorrhea of from Three Months' to Nine Years' Duration.** Dr. Chas. W. Dunn, by invitation. (For original article, see page 186.)

**The Treatment of Abruptio Placentae.** Drs. John A. McGlinn and W. Benson Harer. (For original article, see page 226.)

*MEETING OF MARCH 7, 1935*

The following papers were presented:

**Current Technics for Obstetric Analgesia and Anesthesia.** Dr. C. Gould and Dr. B. C. Hirst. (For original article, see page 257.)

**The Therapeutic Value of Low-Dosage Irradiation of the Pituitary Gland and Ovaries in Functional Menstrual Disorders.** Dr. C. Mazer and Dr. L. Spitz, Jr. (For original article, see page 214.)

**Vaginal Aplasia and Creation of an Artificial Vagina.** Dr. S. L. Israel. (For original article, see page 273.)

**The Primiparous Perineum After Forceps Delivery.** Dr. F. B. Nugent. (For original article, see page 249.)

---

## CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF JANUARY 18, 1935*

*(See also page 151, July issue.)*

The following paper was presented:

**Extrauterine Pregnancy.** Drs. J. E. Fitzgerald and J. J. Brewer. (For original article, see page 264.)

### CASE REPORTS

**Ovarian Pregnancy.** Dr. H. J. Holloway. (See page 286.)

**Human Ovum in a Salpingitis Isthmica Nodosa.** Dr. A. F. Lash. (See page 287.)

*MEETING OF FEBRUARY 15, 1935*

### Symposium on Cesarean Section

The following papers were presented:

**Porro Cesarean Section.** Drs. A. F. Lash and W. G. Cummings. (For original article, see page 199.)

**Cesarean Section: An Analysis of 500 Consecutive Operations.** Dr. Edwin F. Daily. (For original article, see page 204.)

**An Analysis of 381 Cesarean Section Cases in a Ten-Year Period at Michael Reese Hospital.** Drs. I. F. Stein and M. L. Leventhal. (For original article, see page 192.)

### MEETING OF MARCH 15, 1935

The following papers were presented:

**A Series of 627 Vaginal Hysterectomies Performed for Benign Disease With Three Deaths.** Dr. N. Sproat Heaney. (For original article, see page 269.)

**Total Versus Subtotal Abdominal Hysterectomy in Benign Uterine Disease.** Dr. Edward H. Richardson. (For original article see page 237.)

### CASE REPORTS

**Fibromyoma of the Tube.** Dr. Marshall Field.

**Myofibroma of the Ovary with Heteroplastic Bone Formation.** Dr. I. D. Stein. (See page 289.)

**Inversion of the Uterus in Two Successive Pregnancies.** Dr. Paul C. Fox. (See page 295.)

**Lipoma of the Broad Ligament.** Dr. A. E. Kanter. (See page 296.)

**Luker, S. Gordon: Retroversion of the Uterus, Brit. M. J. 2: 760, 1934.**

In classifying the types of retroversion of the uterus the author points out that they are either congenital or acquired. The congenital group in single women may give no symptoms or they may cause symptoms of increasing severity as the patient grows older. Married women with a congenital retroversion may complain of dyspareunia, sterility or miscarriages.

In the acquired group, the cause is usually found in a preceding miscarriage or labor. In the author's experience, 13 per cent of primiparas had retroversion one month after delivery; 3.5 per cent of multiparas.

In discussing the treatment of the congenital type the author states that single women should generally be left alone. In young married women the condition may be treated by manipulation and a pessary and, if symptoms persist and the uterus cannot be replaced, or if the symptoms are ameliorated by a pessary, but the uterus will not remain in the anterior position without the aid of a pessary, then an operation is indicated.

In the treatment of the acquired type, the author stresses prophylactic measures which include adequate bed rest for twelve days with instructions as to posture, immediately following delivery or miscarriage; routine postnatal examinations with correction of any malposition of the uterus by a Hodge pessary; instruction of the patient in suitable exercises to promote involution of the uterus and pelvic floor.

The author then lists the indications for operation as follows: (a) when the retroversion is fixed or is complicated by adhesions or by chronic pelvic inflammation; (b) when the retroversion is giving rise to symptoms which are increasing; (c) when the retroversion, though mobile and simple, causes symptoms which disappear after correction of the displacement and insertion of a pessary; (d) when the retroversion is causing sterility; and (e) when the retroversion is causing miscarriage.

The operation of choice is stated to be the modified Gilliam operation and it is described in detail.

F. L. ADAIR AND I. C. UDESKY.

# American Journal of Obstetrics and Gynecology

---

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.

---

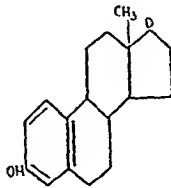
## Editorial Comment

---

### The Relationship Between Estrogenic Substances and Cancer

OF RECENT years there has been a tendency for research work on certain aspects of malignant disease and on the sex hormones to run in parallel directions. Furthermore some writers have claimed that these researches not only run parallel but also tend to converge on common ground, thus implying that the action of the sex hormones may be concerned with the production of malignant disease. It is as well, therefore, that an authoritative statement be made as to the present position of these two important branches of investigation.

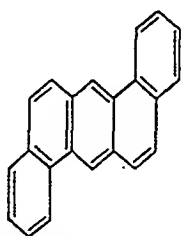
We may begin with the question of sex hormones. Through the work of Allen and Doisy and other American investigators it has been possible to obtain during the last fifteen years a stable form of the estrous-producing hormone which is known to contain only carbon, hydrogen, and oxygen. Mainly through the work of German investigators (Butenandt, et al.) the actual chemical constitution of this substance has been elucidated. It has been shown to belong to the group of organic compounds known as the condensed carbon ring series. The carbon ring skeleton is the same as that occurring in the familiar sterols such as cholesterol, ergosterol, and the bile acids. The constitution is shown in the following formula.



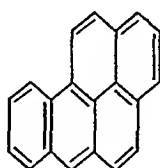
This compound is now available in a pure state in relatively large quantities, and through the work of Kaufmann, an entirely new form of ovarian therapy has been evolved. This employs doses of very much greater magnitude than have hitherto been considered.

If we turn to the field of cancer research, the connection between these apparently separate subjects may be explained. It was originally shown by the Japanese workers, Yamagiwa and Ichikawa that malignant

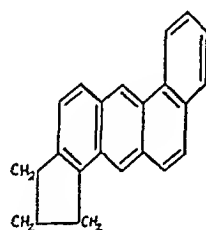
changes could be induced in the skin of mice by the prolonged application of tar. A long and elaborate series of investigations by English workers (Kennaway, et al.) has shown that the carcinogenic principles in tar belong to the condensed carbon ring group of compounds. They have been able to isolate and to synthesize a series of active carcinogenic agents, of which the three main compounds are 1:2:5:6-dibenzanthracene, 1:2-benzpyrene and 5:6-*cyclo*-penteno-1:2-benzanthracene. The formulas of these are given below.



1:2:5:6-dibenzanthracene.



1:2-benzpyrene.

5:6-*cyclo*-penteno-1:2-benzanthracene.

It can be seen that these compounds possess certain points in common with the estrous-producing hormone. They contain a series of six membered carbon rings fused together and most of the compounds contain a phenanthrene nucleus.

A third line of work was commenced by the English group of workers (Cook, Dodds, et al.), who showed that certain simple phenanthrene and dibenzanthracene derivatives were capable of producing estrus in ovariectomized animals. These workers were also able to show that it was possible to have a molecule, such as 5:6-*cyclo*-penteno-1:2-benzanthracene, capable of inducing malignant changes when applied over a long period. Likewise this could produce estrus when injected subcutaneously in very large doses. They also found that even pure caiferol in large doses would develop estrus.

It can well be seen that a superficial knowledge of the subject might lead the untrained observer to suspect that the estrous-producing hormone itself might in fact be capable of causing malignant changes. An extensive search of the literature fails to reveal any incontrovertible evidence that the estrous-producing hormone is carcinogenic. There have been suggestions that injections of very large quantities of estrin would produce metaplastic changes in the uterus, bearing some slight resemblance to precancerous changes. Again too much significance should not be placed on the similarity of molecular structure of these substances. For example, no one would ever suggest that there were possibilities of inducing male changes in women by the injection of the estrous-producing hormone, yet it has a similar molecular structure. It must be remembered that the only difference existing between the male and female sex hormone is that one carbon ring is fully hydrogenated in the former.

E. C. Dodds.

# Department of Reviews and Abstracts

---

CONDUCTED BY HUGO EHRENFEST, M.D.

---

## Selected Abstracts

---

### Uterine Carcinoma

Kolegajew, G. A.: The Etiology and Malignant Degeneration of Leukoplakia of the Cervical Mucosa, *Monatsehr. f. Geburtsh. u. Gynäk.* 93: 166, 1933.

The author examined 3,067 women without the colposcope and found leucoplakia in 15 or once in 204 women.

Leucoplakia develops slowly and without serious symptoms. Only in cases involving the clitoris and the introitus do pruritus and hyperesthesia call attention to it. When in these areas the process is extensive and associated with atrophy it is more often called kraurosis. Sometimes leucoplakia disappears after months or years.

Menstruation causes the epithelium to desquamate and the leucoplakia becomes less distinct but five or six days after the menses there is a return of the prominence of the lesion.

The etiology of leucoplakia is not clear. Some consider it to be due to syphilis and others regard it as a forerunner of cancer. In the author's 28 cases there were inflammatory changes in the uterus and adnexa in 89.2 per cent of all the cases, carcinoma in 3.6 per cent and healthy genitalia in only 7.2 per cent. Not one patient had syphilis. Hence the author believes that the most important etiologic factor is a chronic inflammation. He does not believe that all cases of leucoplakia are forerunners of carcinoma, but cautions that all women with erosions, polyps and leucoplakias should be examined at regular and frequent intervals. When leucoplakia is detected a biopsy should be performed even in the presence of a pregnancy. When doing the biopsy the entire leucoplakic area should be removed in one piece.

J. P. GREENHILL.

Paucot, H.: Cancer of the Cervix and Hereditary Syphilis, *Bull. Soc. d'obst. et de gynec.* page 227, 1934.

The author maintains that inflammatory and chronic lesions of the cervix favor the development of cancer in this area. He, therefore, recommends treatment of inflammations by means of surgical removal or cauterization. He emphasizes particularly that hereditary syphilis plays a rôle in the causation of cervical cancer. In 14 such cases he found evidences of syphilis in 50 per cent. In nearly all the cases, the syphilitic lesions were of the hereditary type.

J. P. GREENHILL.



Graves, Wm. P.: The Detection of the Clinically Latent Cancer of the Cervix, *Surg. Gynec. Obst.* 56: 317, 1933.

The Schiller test is based on the discovery by Lahm that the upper layers of normal epithelium of the portio and vagina contain rich masses of glycogen which disappear when the epithelium becomes cornified or changed by cancer. In the normal living tissue the glycogen of the upper layer of cells is stained in a few seconds a deep mahogany brown by iodine in watery solution (Lugol's). A superficial area of early cancer being devoid of glycogen does not receive the stain and stands out startlingly white or pink against the deeply colored almost black background of the normal tissue.

Any area of the portio no matter how small that does not take the stain must be regarded with suspicion. It then is removed with a specially sharpened spoon curette, placed immediately in hardening solution and sent to laboratory for study.

The test is of limited value in diagnosing advanced cancer, since the superficial assimilation stage is usually lost in the *mêlée* of self-reproducing cells. Sometimes superficial areas detectable by the Lugol test may be found beyond the border of the advanced cancer especially in the fornices of the vagina, and this may serve as a guide in determining the limits for a radical operation. Cancer cells in the advanced stage may regain glycogen and thus give a dark stain with the Lugol's solution. Normal epithelium lying above an invading cancer takes a normal stain as would be expected.

The Schiller test is an indispensable aid in the search for early curable cancer of the cervix. It is specific for the absence of cancer. Failure of the stain indicates certain other abnormal conditions, two of which, leucoplakia and intensive cervicitis, are potential precursors of cancer and require treatment. The test is recommended for trial to the general profession.

WILLIAM C. HENSKE.

Burger, P.: Hemorrhages After the Menopause and Exploratory Curettement, *Gynécologie* 32: 129, 1933.

Postclimacteric hemorrhages except those due to cancer of the cervix are more often due to benign than to malignant conditions. Among the 90 patients observed by the author, the bleeding was due to carcinoma of the cervix in 33.3 per cent, to cancer of the body in 15.6 per cent, to benign conditions in 37.8 per cent, etc. This fact does not diminish the truthfulness of the old axiom that every woman who bleeds after the menopause should be suspected of having cancer; 60 per cent of all his cases had a malignancy. A diagnosis should be made as soon as possible by means of an exploratory curettement.

J. P. GREENHILL.

Hann, K.: The Question of Stump Carcinoma, *Monatschr. f. Geburtsh. u. Gynäk.* 95: 91, 1933.

Hann reports three cases of carcinoma which occurred in the cervical stump after supravaginal hysterectomy. It was decided to examine with the colposcope the cervix of every woman who had had a supravaginal hysterectomy from 1925 to 1931. In a series of 570 such cases, examinations were made in 205 cases. Aside from one case of carcinoma of the stump which was observed irrespective of the colposcopic examination, matrix changes were found in 5 cases. Since the incidence of matrix changes is the same in healthy women as in those operated upon and since carcinoma of the cervix always is engrafted upon matrix changes, the type of operation performed has nothing to do with the development of carcinoma of the cervix.

The author is of the opinion that it is not necessary to perform a total hysterectomy routinely, first because stump carcinoma is uncommon and second because by means of the colposcope we may detect the forerunners of cancer and thereby are enabled to remove the stump early. His recommendation is as follows: Examine every woman with the colposcope before operation. If the cervix is normal, leave it. If matrix changes are observed in the cervix, the latter should be removed by means of amputation through the vagina. These women as well as all others should be colposcoped at least once every year or two. If matrix changes are observed in a cervix after supravaginal hysterectomy it is simple to remove the cervix extra-peritoneally.

J. P. GREENHILL.

---

### Diseases of Respiratory and Circulatory Systems and Intestinal Tract Complicating Pregnancy

Lamb, A. E.: Heart Disease in Pregnancy, *Am. J. M. Sc.* 187: 177, 1934.

The incidence of cardiac murmurs in pregnant women in this series was 6.1 per cent. Of these 2.7 per cent had organic heart disease, while 3.4 per cent had only functional murmurs and no detectable lesion. None of these patients showed the slightest evidence of cardiac strain during pregnancy, and follow-up studies showed that nearly all of these functional murmurs disappeared after delivery. Rheumatic heart disease causes about 90 per cent of the heart lesions in pregnant women. The most frequently observed lesion is mitral stenosis with or without insufficiency. A third of the cases of mitral stenosis became decompensated, while no case of uncomplicated mitral insufficiency decompensated, demonstrating the importance of differentiating between these two lesions. It was noted that five patients out of those with or without organic heart disease, who were able and unable to carry on ordinary physical activity without discomfort, decompensated, which is at variance with the work of Pardee, who asserts that these patients have an excellent prognosis. Outside of functional classification, other factors such as age of the patient, family environment, duration of the heart disease, and the extent of the valvular lesion must be considered. Most of the patients who decompensated did so before the onset of labor, and there was no relationship demonstrated between the month of pregnancy and the onset of decompensation. The mortality was 7.5 per cent; two of these deaths were probably preventable. Comparison of the mortality of patients with and without prenatal care shows a death rate of 2.2 per cent for the former, and 20 per cent for the latter, demonstrating the importance of prenatal care. The limited follow-up showed that 43 per cent were worse following pregnancy.

J. THORNWELL WITHERSPOON.

Gilchrist and Murray-Lyon: Does Pregnancy Hasten the Fatal Termination in Rheumatic Heart Disease? *Edinburgh M. J.* 40: 587, 1933.

Pregnancy and labor impose a burden on the healthy heart. For this reason the symptoms of preexisting organic heart disease become, as a rule, greatly accentuated as pregnancy advances.

A study has been made of 109 cases of fatal cardiac rheumatism in an endeavor to discover the effect of repeated pregnancies on the course of the disease. A comparison has been made between males, nulliparous and parous women regarding their average age at death, mode of dying, duration of the cardiac disease and the rate of progression to the fatal termination.

All the patients suffered from mitral stenosis either alone or in association with other valvular lesions. No significant difference was found in the duration of the disease in nulliparous and parous women. The course of the disease appeared to be shorter in the male cases.

Auricular fibrillation is not necessarily an indication that an additional burden has been placed upon the heart during the childbearing period. Its incidence is largely determined by the length of survival from the time of the first involvement of the heart.

Congestive heart failure was the mode of death in 92 per cent of the whole group of cases. The fact that the parous women dying from congestive heart failure had families averaging 4.5 children each would support the contention that repeated childbearing accelerated their death.

Cerebral embolism accounted for all the remaining deaths with two exceptions. Parous women, dying from this cause, lived on the average twelve years longer than those who died from congestive heart failure. In spite of their longer life, their families only averaged 1.7 children. It would appear that by escaping the burdens of a large family they guard themselves against the risk of congestive heart failure at about thirty-eight years of age, only to die from embolism twelve years later. This appears to be about the maximum span of life for the individual dying from rheumatic heart disease.

While pregnancy should be avoided in the severer grades of rheumatic heart disease, one or two children may be borne without detriment by the majority of cardiac women. Repeated pregnancies, however, tend to shorten life in women suffering from rheumatic heart disease and ultimately increase the risk of death from congestive heart failure.

WM. C. HENSKE.

Marbury, W. B.: Appendicitis in Pregnancy, *Am. J. Surg.* 19: 437, 1933.

Primary acute appendicitis occurs probably no more frequently in pregnant than in nonpregnant women. On the other hand, pregnancy is likely to cause an exacerbation of a previously pathologic appendix. Over 80 per cent of the reported cases occurred during the first six months. In nonsuppurative cases during the first six months the outlook for both mother and child is excellent. Later, the mortality increases parallel to the duration in months of pregnancy and duration in hours of the appendicitis. The first symptom is the constant contraction of the uterus that may occur as the result of appendicitis and can be so severe as to simulate the onset of labor. It is largely this symptom that makes it almost impossible to diagnose appendicitis after labor begins. The other deceptive factor is the displacement of the abdominal viscera by the growing uterus. The appendix is pushed up almost to the level of the gallbladder. Pain from a pathologic appendix in this area would be exceedingly difficult to distinguish from that produced by an inflamed gallbladder, a pleurisy, a renal colic or even a duodenal ulcer. Appendical pain must be sought at progressively higher levels as the months of pregnancy pass by. Pyelitis on the right side is the most frequent cause of error. It can coexist with acute appendicitis and should be either ruled out or definitely determined by ureteral catheterization. Other conditions that may cloud the picture are salpingitis on the right side, tumors of the adnexa, ovarian tumors with twisted pedicle, criminal interference, and intestinal obstruction.

There is little divergence of opinion among authors as to prompt operation during the first six months of pregnancy. After this, a complicating appendicitis is a surgical as well as obstetric problem, and since a mortality between 18 and 70 per cent is faced there is small wonder that there is less agreement. If unruptured, the appendix can be removed through a simple McBurney incision, and the chances

of aborting are slight. If there is a localized abscess the same procedure may be followed but there is much greater chance of abortion. If abortion occurs the change in the size of the uterus breaks up what protective adhesions have formed and allows the peritonitis to become generalized. Consequently it may be wiser to make a paramedian incision and empty the uterus by cesarean section first and deal with the appendix secondarily. Where generalized peritonitis is revealed at the time of exploration, infection of the endometrium is inevitable, therefore a Porro cesarean section should be done.

J. THORNWELL WITHERSPOON.

Gröné, O.: Perforation of the Stomach Associated With Approaching Labor. Cancer and Ulcer of the Stomach as Complications of Labor, *Acta obst. et gynec. Scandinav.* 13: 315, 1934.

The author describes a case of perforation of the stomach three or four weeks before expected delivery. After the diagnosis had been confirmed by laparotomy, the uterus was emptied by vaginal cesarean section (living child), and then the perforating ulcer in the stomach sutured with catgut. Neither peritonitis nor puerperal septicemia set in, but the patient died, under increasing cachexia, about three weeks after admission. The necropsy showed infiltrating cancer in the margin of a gastric ulcer.

Discussing the question of perforating peritonitis in connection with pregnancy, the author believes that immediate emptying of the uterus, in connection with an operation for perforating peritonitis, should be resorted to only in those cases where the size of the pregnant uterus prevents examination of the starting point for the peritonitis, and thus the rational treatment of the latter. From the viewpoint of aseptic surgery, vaginal cesarean section is the correct procedure but the author mentions several cases from literature, in which the uterus, in connection with laparotomy for peritonitis, was emptied abdominally without causing puerperal septicemia. The author briefly explains the reciprocal relation between carcinoma of the stomach and pregnancy and finally discusses the question of gastric ulcer in relation to pregnancy and delivery, pointing out especially that in connection with the delivery itself such alarming symptoms may arise from the latter, that special and immediate therapeutic measures become necessary. Among such symptoms he mentions particularly perforation of the ulcer into the free abdominal cavity, abundant gastric hemorrhage and pernicious vomiting. He illustrates these various complications by cases from his own experience. In one such, where there was abundant gastric hemorrhage, he performed an abdominal cesarean section; in another, where stenosis of the pylorus was the cause of vomiting, he induced premature delivery. In both cases good results were obtained. In another case it seemed proved that the delivery had a directly unfavorable influence on an organic stomach affection arising from a gastric ulcer.

J. P. GREENHILL.

---

### Erratum

In the article by Robinson in the July issue, page 34, the second last line should read "the thyroid inhibits prolactin A elaboration, and the adrenal that of prolactin B."

## Books Received

---

PRACTICAL ENDOCRINOLOGY. By Dr. Max A. Goldzieher, Endocrinologist, Gouvernor Hospital, etc. Illustrated and 326 pages. D. Appleton-Century Co., Inc., New York, 1935.

PRACTICAL SURGERY OF THE ABDOMINAL AND PELVIC REGIONS. By James William Kennedy, Surgeon-in-Chief to the Joseph Price Hospital, etc. Second edition, illustrated with 133 original half-tone plates, some in color, and 861 pages. F. A. Davis Company, Philadelphia, 1934.

WEIBLICHE GESCHLECHTSORGANE UND UNFALL. Von Professor Dr. August Mayer, Direktor der Universitäts-Frauenklinik in Tübingen. 83 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

ELEMENTS OF EXPERIMENTAL EMBRYOLOGY. By Julian S. Huxley and G. R. de Beer. With 221 illustrations and 514 pages. Cambridge University Press—The Macmillan Co., New York, 1934.

THE AUTONOMIC DISEASES OR RHEUMATIC SYNDROME. By Dr. T. M. Rivers. 299 pages. Dorrance & Company, Inc., Philadelphia, 1934.

PHYSICAL AND MENTAL GROWTH OF PREMATURELY BORN CHILDREN. By Julius H. Hess, Professor of Pediatrics, University of Illinois; George J. Mohr, Director of Child Guidance Center in Pittsburgh; and Phyllis F. Bartelme, Psychologist, Cook County Juvenile Court in Chicago. 449 pages. University of Chicago Press, 1934.

TREATMENT OF COMMON FEMALE AILMENTS. By Frederick John McCann, Consulting Surgeon, Samaritan Free Hospital for Women, London, etc. Third edition, 379 pages. William Wood & Co., Baltimore, 1934.

ANESTHESIA AND ANALGESIA IN LABOUR. By Katharine G. Lloyd-Williams, M.D., Honorary Anaesthetist to the Royal Free Hospital in London, etc. With foreword by Dame Louise McIlroy, Professor of Obstetrics and Gynaecology, London School of Medicine for Women. 96 pages. William Wood & Co., Baltimore, 1934.

PROFÉDEUTIQUE OBSTÉTRICALE. Par L. Devraigne, accoucheur de Lariboisière. 191 pages. Masson et Cie, éditeurs, Paris, 1934.

LA PRATIQUE OBSTÉTRICALE. Par L. Devraigne, accoucheur de Lariboisière. 244 pages. Masson et Cie, éditeurs, Paris, 1935.

TEXTBOOK OF NURSING TECHNIQUE. By Marion L. Vannier, R.N., and Barbara A. Thompson, R.N., Director of the Wisconsin Bureau of Nursing Education, etc. Second edition, revised, 265 pages. University of Minnesota Press, Minneapolis, 1935.

MANOBRAS E OPERACOES OBSTÉTRICAS, pelo Docente Dr. Joao Pereira de Camargo, Livre Docente da Faculdade de Medicina da Universidade do Rio de Janeiro, etc. Segunda edição correcta e augmentada, contendo 15 trichromias, 242 clichés e 4 microphotographias. 498 pages. Livraria Francisco Alves, Rio de Janeiro, 1935.

INTRODUZIONE ALLO STUDIO DELL' EUGENICA (Eredità biologica). Par Prof. Giuseppe Cristalli. Stabilimento Industrie Editoriali Meridionali, Napoli, 1934.

# American Journal of Obstetrics and Gynecology

---

VOL. 30

ST. LOUIS, SEPTEMBER, 1935

No. 3

---

## Original Communications

---

### PHYSIOLOGY OF THE CORPUS LUTEUM\*

#### THE COMPARATIVE ACTIONS OF CRYSTALLINE PROGESTIN AND CRUDE PROGESTIN ON UTERINE MOTILITY IN UNANESTHETIZED RABBITS

WILLARD M. ALLEN, M.D., ROCHESTER, N. Y., AND SAMUEL  
R. M. REYNOLDS, M.A., PH.D., BROOKLYN, N. Y.

*(From the Department of Obstetrics and Gynecology, University of Rochester School  
of Medicine and Dentistry, and the Department of Physiology,  
Long Island College of Medicine)*

IN A PREVIOUS paper (Reynolds and Allen, 1932) we showed that corpus luteum extracts containing impure progestin inhibit spontaneous estrus uterine motility in the unanesthetized rabbit, and that similar extracts will inhibit the motility which follows the intravenous injection of theelin. These results were but part of a series of experiments (see Reynolds and Allen, 1932) demonstrating the rôle of estrin in the induction of uterine motility and that of the corpus luteum in the inhibition of such motility. These experiments showed that suitable corpus luteum extracts would inhibit estrous motility in the same manner as the corpus luteum itself. We were unable to say at that time, however, whether the inhibiting principle was identical with the hormone causing progestational proliferation of the endometrium (progestin), or whether a separate active principle was involved because no attempt was made to study any fractions except those known to contain progestin.

---

\*Aided in part by a grant from the Therapeutic Research Committee of the American Medical Association. This is number X of a series of studies dealing with the Physiology of the Corpus Luteum.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

We also found that inhibition of estrous motility could be obtained in the absence of proliferation if pseudopregnant rabbits were given 200 rat units of estrin per day for the first five days after mating. Under these circumstances proliferation failed to occur, presumably because of the large amount of estrin being injected even though healthy appearing corpora lutea were present in the ovaries, and at the same time the uterus became quiescent. These results could, of course, be used as evidence favoring two hormones, one causing proliferation (progesterin), and another bringing about uterine quiescence. However, the motility-inhibiting factor was shown to be destroyed by treatment with alkali, in this respect being similar to crude progesterin.

Considerable evidence of another type having a bearing on the possibility of a second corpus luteum hormone has appeared from several laboratories, all based on Knaus' (1930) original observation that progesterin or at least corpus luteum extracts made by the method of Corner and Allen (1929), and known to contain progesterin, cause inhibition of the response of the uterus to pituitrin in vitro. Knaus made no attempt to determine by quantitative analysis of the various fractions whether nonprogesterin-containing fractions might contain the pituitrin-inhibiting substance to the exclusion of progesterin, but work by Robson and Illingworth (1931), Tausk, de Fremery, and Luehs (1931), Fevold and Hisaw (1932) shows that such fractions can be prepared. The first two groups of workers were able by distributions between suitable solvents to get an apparent separation of two principles, and Fevold and Hisaw found that their active progesterin-containing crystals had no pituitrin-inhibiting capacity. Further evidence for two hormones is to be found in experiments of another type by Robson. He (1932 *a, b*) has shown that when daily injections of anterior lobe tissue are given to female rabbits for several days, corpora lutea are formed and pregestational proliferation takes place as would be expected, but curiously enough the uterus does not become refractory to pituitrin, and vice versa, that occasionally after prolonged administration a dissociation may occur in which pituitrin inhibition occurs in the absence of proliferation. It should be added that this dissociation does not occur when a single injection of anterior pituitary extract or pregnancy urine is given.

From the above considerations, it is apparent that pituitrin inhibition in vitro and motility inhibition in vivo may not be due to progesterin but rather to a second corpus luteum hormone (called *desensin* by Tausk). Consequently a joint research was made by Tausk and Reynolds, studying the effects of the same fractions by both methods to see if pituitrin-inhibiting fractions which did not have good proliferating capacity would inhibit in vivo motility and vice versa (Tausk, de

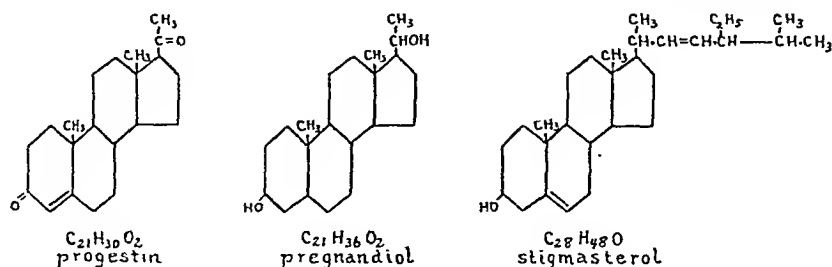
Fremery, Luchs, and Reynolds, 1934). The results were inconclusive in that both fractions inhibited spontaneous motility in vivo. It was evident, therefore, that proof of two distinct hormones was not forthcoming from these experiments and that more conclusive evidence would probably have to await the isolation of pure progesterin or pure desensin. Now that crystalline progesterin has become available,\* answers to these questions can be expected.

In this paper we shall make a comparison of the effects of the two forms of crystalline progesterin with each other and with less pure progesterin as determined by their capacity to suppress the estrous type of motility in vivo.

#### EXPERIMENTAL

*Extracts.*—The crystalline preparations were made by methods similar to those recently published (Wintersteiner and Allen, 1934). The details need not be given here. The preparation designated in the subsequent experiments as 104-B was made up of 4.43 mg. of the B type, a pulverized sample of which melted at 123° to 125.5°, and which had an elementary constitution of C, 80.16 per cent and H, 9.68 per cent (theoretical for  $C_{21}H_{30}O_2$ , H 9.62 per cent). These crystals were not quite pure because after several more crystallizations the melting point was 127° to 128°. Such recrystallization did not appreciably alter the combustion figures or the physiologic activity. The preparation designated as 110-C consisted of 4.70 mg. of C-type crystals which melted at 120.5° to 121° and which had an elementary constitution of C, 79.58; H, 9.85.† These can be considered practically pure. The first compound (104-B) gave ++++ proliferation with 1.33 mg., ++ with 0.88 mg., and + with 0.44 mg., and the second compound ++++ with 1.28 mg., ++ with 0.94 mg., and + with 0.63 mg. when assayed by the Corner-Allen method (Corner and Allen, 1929; Allen, 1930). We considered 1.33 mg. and 1.28 mg. as a rabbit unit, respectively. For the impure progesterin we deliberately chose one of the fractions

\*Recently progesterin has been isolated in pure form (Wintersteiner and Allen, 1934; Slotta, Ruschig and Fels, 1934; Butenandt, Westphal, and Holweg, 1934; Hartmann and Wettstein, 1934.) It occurs in two crystal forms: one, long needles melting at 120° to 121° and the other, short, blunt prisms melting at 128°. Both forms have the same physiologic activity as determined by their capacity to produce gestational proliferation in the rabbit. The hormone itself is an unsaturated diketone,  $C_{21}H_{30}O_2$ , which absorbs ultraviolet with a maximum at 240 $\mu$ . It is closely related to pregnandiol ( $C_{21}H_{32}O_2$ ) and has been prepared synthetically from this compound, (Butenandt and Schmoldt, 1934) and from stigmasterol (Fernholz, 1934.). These observations indicate without much question that the formula suggested by Slotta, Ruschig, and Fels (1934), and Butenandt, Westphal, and Cobler (1934) is correct.



†It will be noted that the combustion figures for this type show a little less carbon than the B type. This has been a more or less consistent finding and probably indicates incomplete combustion of the carbon.

We wish to express our gratitude to Dr. O. Wintersteiner for the separation of these two crystalline compounds by fractional crystallization and for the microanalyses. Without his generous cooperation, this paper would have been impossible at the present time.



which is usually discarded (or set aside) in the preparation of crystals, because it contains very little progesterin but a relatively large amount of solids. Such a fraction is obtained when a moderately pure extract is distributed between 70 per cent ethyl alcohol and petroleum ether. The preparation designated as 104-K was prepared by shaking a petroleum ether solution of the hormone several times with 70 per cent ethyl alcohol, the petroleum ether fraction being used for the impure fraction (104-K) and the 70 per cent fraction (which contained most of the hormone) being further purified. This fraction contained 43 mg. of solids per rabbit unit.

*Rabbits.*—The rabbits used were of chinchilla or albino stock, weighing 2.8 kg.  $\pm$  200 gm. whose sexual maturity was proved either by impregnation following mating, or ovulation after a single intravenous injection of pregnancy urine. In the first two groups of experiments recounted below (104-K and 104-B), the animals were used from one to three weeks *postpartum*, a uterine fistula being prepared (for method, see Reynolds and Friedman, 1930), and bilateral oophorectomy being done from three to six days prior to the actual experiments. The rabbits used in the study of 110-C were, for convenience, prepared in a slightly different manner. They were injected intravenously with 10 e.e. of human pregnancy urine and the fistulas pre-

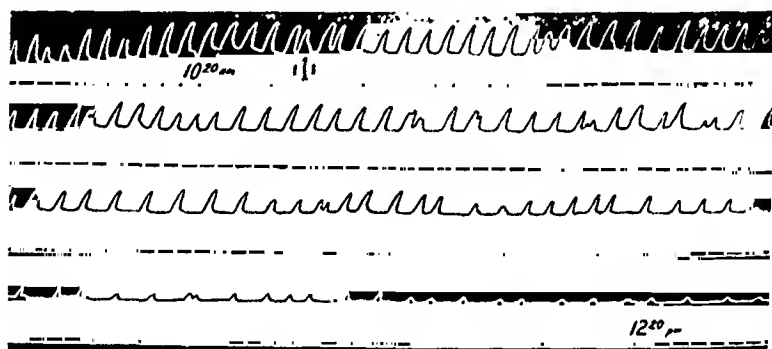


Fig. 1.—Inhibiting action on *in vivo* uterine motility of 0.6 rabbit unit (25.8 mg.) of impure progesterin-containing corpus luteum extract. Extract given at 1. Inhibition of motility in slightly less than two hours.

pared and bilateral oophorectomies done six to eight days later, the motility experiments being done four to seven days after these operations. Records of uterine contractions in all cases were obtained by the use of a small intrauterine balloon connected to a Brodie bellows through an air-water system in such a way that the balloon was under virtually uniform distending tension (20 cm. water) (technic, Reynolds, 1930; Reynolds and Friedman, 1930).

*Experimental Procedure.*—The experimental procedure was as follows: on the day before a test, 100 R.U. of theelin\* were administered in three divided doses, half intravenously and half subcutaneously. Such injections faithfully induce rhythmic uterine contractions which attain a maximum in twenty-four hours (Reynolds, 1931). This motility supplied a fairly standard background against which the inhibiting action of the extracts might be shown. The next day the balloon was inserted for twenty to thirty minutes before actual recording was begun, to allow time for subsidence of the disturbing effect attendant upon securing the animal to a board and recording. The drum was then started and after sufficient time had elapsed to show the degree of uniformity in the type of contractions, the desired amount of progesterin, measured in rabbit units and diluted to one cubic centimeter with saline, was sub-

\*We are indebted to Parke, Davis, and Company for the theelin used.

cutaneously injected in the left lower quadrant. A continuous record was made following the injection until there was complete inhibition of motility (Figs. 1 and 3) or until the character of the contractions had become undulating or arrhythmic (Fig. 2). The absolute end point was not always easy to determine and in some cases a certain amount of arbitrary judgment had to be employed. When the uterus becomes virtually quiescent, as in Figs. 1 and 3, there is little doubt as to when the minimum motility has been reached. Occasionally, however, all rhythmicity is lost, but long

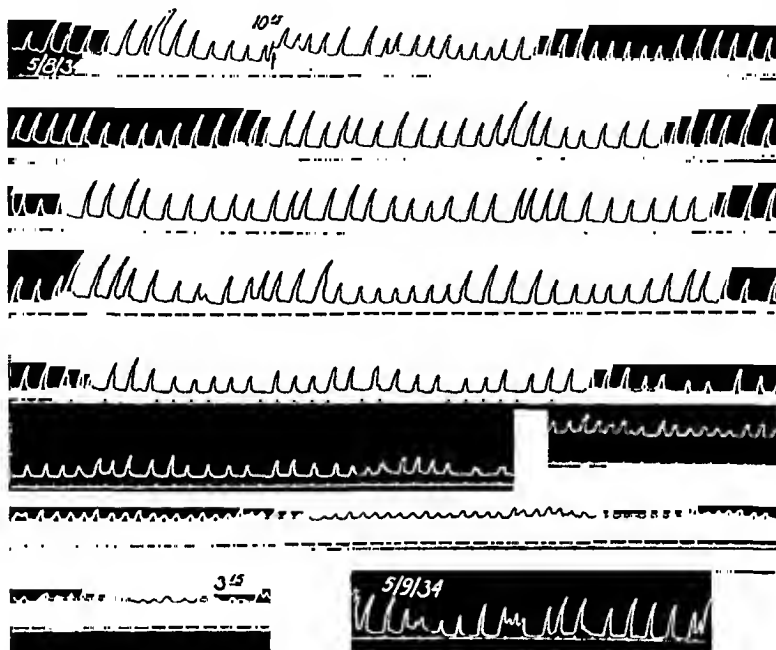


Fig. 2.—Inhibiting action of 0.2 rabbit unit (0.26 mg.) of crystalline progesterin B (m.p.  $127^{\circ}$ - $128^{\circ}$ ) on in vivo motility. Progesterin injected at 10:15. Inhibition was obtained in five hours. The arrow indicates a slight shift in the position of the rabbit, with a temporary elevation from the base line. The interruption in the sixth line indicates when the rabbit struggled loose after more than four hours of recording. The balloon was promptly replaced and the recording continued. Note that the inhibition was temporary, since motility was resumed by the next day, May 9.

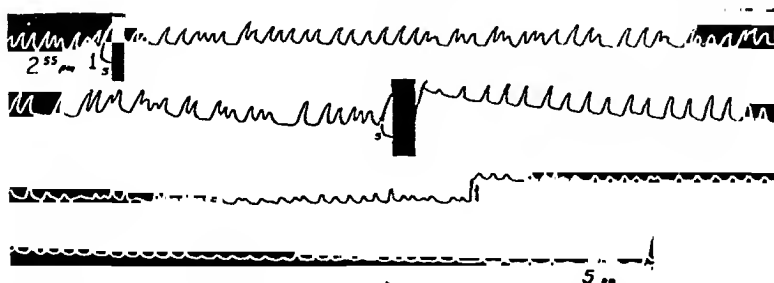


Fig. 3.—Inhibiting action of 0.6 rabbit unit (0.77 mg.) of crystalline progesterin C (m.p.  $120^{\circ}$ - $121.5^{\circ}$ ) on uterine motility. Progesterin given at 1. Rabbit struggled loose at S and again at S in the next line. The balloon was promptly replaced each time. Inhibition occurred in two hours.

uneven contractions of variable duration persist. In such cases it is our practice to continue the record for an indefinite period, to make certain that the motility will not become less within a reasonable length of time and then, if such irregular motility persists, the end point or inhibition time is considered to be the time of the onset of the disordered activity. Data from such experiments give inhibition times which correspond very well with those observations in which quiescence supervenes.

In a number of experiments records were obtained the day following the experimental procedures. At this time it was invariably observed that the small amounts of progestin used in these experiments did not prevent a return to estrous rhythm within twenty-four hours (Fig. 2).

### RESULTS

Experiments carried out along the lines laid down above yielded the following results:

*Crude Progestin-Containing Extract (104-K).*—Of 32 experiments conducted after a number of preliminary trials, 14 were performed with the use of 0.3 Rb.U. of progestin, 15 with 0.6 Rb.U., and 3 with 1.2 Rb.U. The results are represented graphically in Fig. 4. There it may be seen that the average inhibition times for the three doses, respectively, correspond inversely to the dosage employed. The average for 1.2 Rb.U. is just under an hour; for half this dose, a little over two

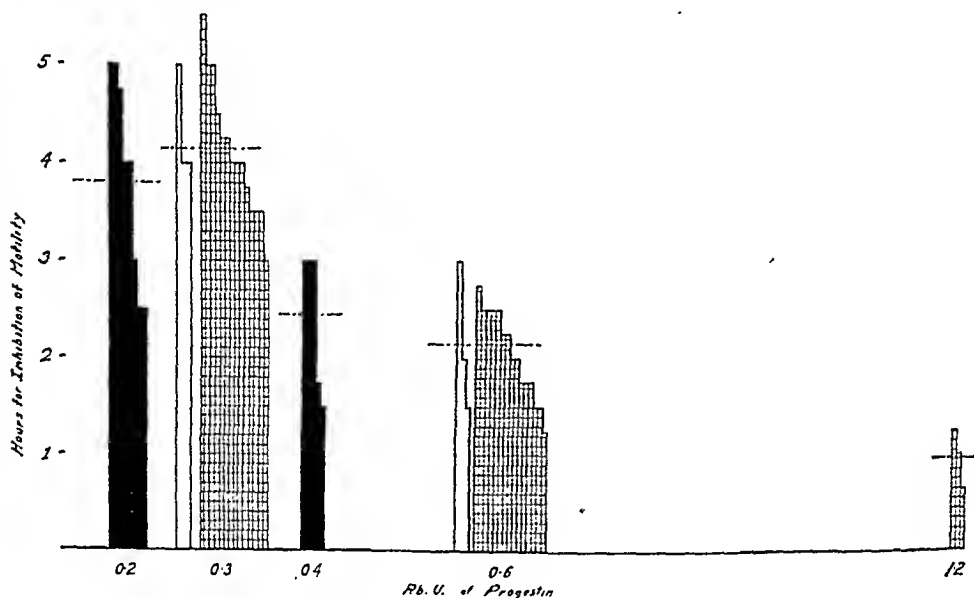


Fig. 4.—Composite chart showing the individual inhibition times in all experiments with each preparation. Solid black, crystalline progestin B; white, crystalline progestin C; latticed, crude progestin. The transverse line through each column represents the average inhibition time for each group, respectively.

0.2 rabbit unit progestin B, 8 rabbits; 0.3 rabbit unit progestin C, 3 rabbits; 0.3 rabbit unit crude progestin, 14 rabbits; 0.4 rabbit unit progestin B, 5 rabbits; 0.6 rabbit unit progestin C, 3 rabbits; 0.6 rabbit unit crude progestin, 15 rabbits; 1.2 rabbit units crude progestin, 3 rabbits.

hours, and for one-fourth the larger amount, the inhibition time is slightly over four hours. That is to say, as far as average times are concerned, one-fourth the maximal dosage requires four times as long as the maximal dosage to effect inhibition of the rhythmic contractions brought on by estrin. A glance at Fig. 4, however, reveals that this is true only when one speaks of average times, owing to the range of inhibition times within each group.

Inasmuch as the injections were made by dilution of an alcoholic solution of the hormone it was deemed advisable to determine the effect of alcohol on the time required for inhibition. The largest dose of progestin given, 1.2 Rb.U., contained four times as much alcohol as the smallest amount, 0.3 Rb.U. (ca. 0.6 c.c. of alcohol in the former and 0.15 c.c. in the latter). Therefore experiments were carried out to test the effect of the various amounts of alcohol used. Two animals were each given 0.6 c.c. of alcohol, and in each case the preinjection motility continued un-

altered for four to five hours, the period of observation. Another animal was given 0.15 c.c. of 104-K in combination with 0.45 c.c. of alcohol, thereby receiving the smallest dose of hormone (0.3 Rb.U.) given in the regular series, but at the same time a quantity of alcohol equal to that given to the animals getting 1.2 Rb.U. The inhibition time was four hours, i.e., the same as for those getting 0.3 Rb.U. in 0.15 c.c. alcohol. A fourth animal was injected with 0.3 c.c. (0.6 Rb.U.) of the extract plus 0.3 c.c. of alcohol, and in this case the inhibition time was two and one-fourth hours. It is evident, therefore, that alcohol per se does not cause inhibition of motility, and that the doses given have no effect on the time required for the development of quiescence when graded amounts of hormone are injected.

*Crystalline Progesterone B* (104-B, mp. 123.5°-125.5°).—In all, eight experiments with 0.2 Rb.U. (0.26 mg.) each and five with 0.4 Rb.U. (0.53 mg.) each were performed. As may be seen in Fig. 2 and in the chart, Fig. 4, inhibition of rhythmic uterine motility occurred with this form of the pure hormone. The average inhibition times were found to be, as shown in Fig. 4, nearly four hours for 0.2 Rb.U. and just under two hours and a half for the 0.4 Rb.U. dosage. The extent of the range of variation of inhibition times in both of these groups is no greater than the range of variation in the 0.3 Rb.U. series in which crude extract (104-K) was used.

*Crystalline Progesterone C* (110-C, mp. 120.5°-121°).—Six successful experiments have been performed with the available material of this preparation, three with a dosage of 0.3 Rb.U. (0.38 mg.), and three with a dosage of 0.6 Rb.U. (0.77 mg.). A seventh experiment was attempted but due to a faulty balloon, atypical results were obtained as described below. The inhibition times for 0.3 Rb.U. were three and three-fourths hours, three and three-fourths hours, and five hours, respectively. With the higher dosage of 0.6 Rb.U., the inhibition times were one and one-half hours, two hours, and three hours.

The only experiment in which inhibition failed to occur in a total of fifty-two was one of this series. Six-tenths of a rabbit unit of preparation C was used after the control period had shown marked uterine motility. When the injection was made, the rabbit struggled loose and broke the balloon at the same time. This was replaced and the experiment continued. As time passed, the contractions became greater and greater. The peak of the contractions did not become elevated, but the increase in amplitude continued progressively over a period of nearly five hours at the expense of the base level, as the tone diminished. When the experiment was terminated, it was found that the new balloon had become weakened on one side and was distended so that the capacity was increased to several times its normal size. Evidently, as in certain other physiologic systems (e.g., the heart), the increase in volume of the bolus within the uterus and consequent lengthening of the muscle fibers increases the irritability of the uterus and at the same time greatly enhances the efficiency of the otherwise weakened contractions.

#### SUMMARY

The injection of varying doses of either form of crystalline progesterone or of a partially purified progesterone fraction into castrated rabbits in which the estrous type of uterine motility has been induced by the injection of theelin causes cessation of all rhythmic contractions, as recorded without anesthesia by an intrauterine balloon. Graded injections (0.3 Rb.U., 0.6 Rb.U., 1.2 Rb.U.) of impure progesterone cause inhibition of motility in four hours ( $\pm 1$  hour), two hours ( $\pm 45$  minutes), and

fifty-five minutes ( $\pm 15$  minutes), respectively. Crystalline progestin B, with doses of 0.2 Rb.U. and 0.4 Rb.U., and crystalline progestin C, with 0.3 Rb.U., and 0.6 Rb.U., bring about cessation of motility in approximately the same time as similar doses of the impure preparation.

#### DISCUSSION

It is clear that the foregoing results obtained with the use of crystalline progestin bear conclusively upon the problem of the possible diversity of action of various progestin fractions. They show, for example, that crystalline progestin in either the B or C form inhibits estrin-induced rhythmic contractions of the uterus in the castrated rabbit. Moreover, the data show that not only are both forms of progestin endowed with the inhibitory function, but when progestin-containing extracts are increasingly purified, there occurs simultaneously a proportionate increase in concentration of the hormone responsible for inhibition of motility. Thus we are forced to the conclusion that *the two hormonal effects, endometrial proliferation* (already shown to be produced by either form of crystalline progestin, Wintersteiner and Allen, 1934) *and inhibition of estrous motility, are attributable to the single hormone, progestin.* On the other hand, the results do not answer the question of whether inhibition of pituitrin responses of the uterus in vitro is due to progestin or a second hormone. Solution of that problem will have to await actual experiments, using crystalline progestin.

When this work was undertaken, the thought was entertained that the uterine fistula technic might lend itself to standardization of progestin preparations. The variation of inhibition times for the respective dosages with no sharp delineation between the shortest inhibition time of one group and the longest inhibition of the next group renders this method inapplicable, however. With unknown dosages this would present a serious difficulty. Still another objection to the fistula method lies in the fact that substances other than progestin inhibit estrous motility (prolan and certain anterior pituitary extracts, Reynolds, 1932a; 1932b). Unless one knows, therefore, that pure progestin is being used, one cannot rely upon inhibition alone as a test for progestin. Accordingly these and other considerations make it obvious that the preferred biologic method for standardization of progestin continues to be the Corner-Allen method of histologic assay.

These experiments, together with those which we have reported previously, using crude progestin-containing extracts (Reynolds and Allen, 1932), provide the scientific basis for the suggested use of progestin in certain forms of dysmenorrhea. Its possible use in this condition is very attractive; strong uterine contractions, which in laboratory animals are known to occur only when under the influence of estrin, presumably

account for the crampy pain of severe dysmenorrhea in some instances; assuming that these contractions are due to estrin, the same as in rabbits, progestin would be expected to alleviate the symptoms. The dose necessary should not be great; in fact it should of necessity be less than the amount necessary to produce a premenstrual endometrium, since the injection of such an amount would probably delay the onset of the menstrual period rather than alleviate the cramps. That such a possibility is a real one is shown by experiments in monkeys in which progestin is known to delay an experimentally induced menstrual period (Smith and Engle, 1932) as well as a normal period (Corner, 1935). Some basis for this opinion regarding dosage is found in our own experiments with rabbits: a single subcutaneous injection of 0.2 rabbit unit will bring about complete quiescence in about five and one-half hours while a similar dose must be given for five days to bring about full gestational growth of the endometrium (Reynolds and Allen, 1932). The exact amount necessary for human use cannot, of course, be deduced from these experiments, but one would not expect it to be great when we consider the fact that Kaufmann (1933) has produced a premenstrual endometrium with from 35 to 90 rabbit units. The fact that crystalline progestin ( $C_{21}H_{30}O_2$ ) causes this inhibition of motility in a manner identical with crude extracts has considerable clinical bearing also, because the hormone will probably be supplied in the synthetic form rather than in the naturally occurring form.

The use of progestin in other conditions such as habitual and threatened abortion, premature labor, and hyperplasia of the endometrium seems less certain of success but nevertheless worthy of trial (see Krohn, Falls, and Laekner, 1935). In abortions, many times, the termination of the pregnancy is secondary to an abnormal embryo, but there are in all probability some cases in which the abortion is due to an exceptionally irritable uterine muscle; in such cases and in premature labor, not associated with mechanical defects such as rupture of the membranes, progestin might be beneficial. Its suggested use in hyperplasia is based on the well-known observation that in most cases this condition is associated with absence of corpora lutea.

#### CONCLUSIONS

Purification and concentration of impure progestin-containing extracts of corpora lutea, with ultimate crystallization of progestin, are accompanied by a simultaneous and proportionate increase in the two hormonal effects, endometrial proliferation and inhibition of uterine motility in unanesthetized rabbits. It is evident, therefore, that these are dual properties of the single hormone, progestin.

The bearing of this work on certain clinical problems is discussed.

## REFERENCES

- Allen, W. M.: *Am. J. Physiol.* 92: 174, 1930. Allen, W. M., and Wintersteiner, O.: *Science* 80: 190, 1934. Butenandt, A., and Westphal, U.: *Berichte* 67: 1440, 1934. Butenandt, A., Westphal, U., and Cobler, H.: *Berichte* 67: 1611, 1934. Butenandt, A., Westphal, U., and Holweg, W.: *Hoppe-Seyler's Ztschr. f. phys. Chem.* 227: 84, 1934. Butenandt, A., and Schmidt, J.: *Berichte* 67: 1901, 1934. Butenandt, A., and Schmidt, J.: *Berichte* 67: 2088, 1934. Corner, G. W.: Unpublished experiments, 1935. Corner, G. W., and Allen, W. M.: *Am. J. Physiol.* 88: 326, 1929. Fernholz, E.: *Berichte* 67: 1855, 1934. Fevold, H. L., and Hisaw, F. L.: *Proc. Soc. Exper. Biol. & Med.* 29: 620, 1932. Fremery, P. de, Luchs, A., and Tausk, M.: *Pflüger's Arch.* 231: 341, 1932. Hartmann, M., and Wettstein, A.: *Helv.* 17: 878, 1934. Hisaw, F. L.: Chap. XI in *Sex and Internal Secretions*, Baltimore, 1932, Williams & Wilkins Co. Kaufmann, C.: *Klin. Wehnsehr.* 12: 1557, 1933. Knaus, H.: *Arch. Exper. Path. u. Pharmacol.* 161: 371, 1930. Krohn, L., Falls, F., and Lackner, J. E.: *Am. J. OBST. & GYNEC.* 29: 198, 1925. Reynolds, S. R. M.: *Am. J. Physiol.* 92: 420, 1930; *Am. J. Physiol.* 97: 706, 1931; *Am. J. Physiol.* 100: 545, 1932(a); *Proc. Soc. Exper. Biol. & Med.* 30: 59, 1932(b). Reynolds, S. R. M., and Friedman, M.: *Am. J. Physiol.* 94: 696, 1930. Reynolds, S. R. M., and Allen, W. M.: *Am. J. Physiol.* 102: 39, 1932. Robson, J. M.: *Quart. J. Exper. Physiol.* 22: 7, 1932(a); *Quart. J. Exper. Physiol.* 22: 209, 1932(b). Robson, J. M., and Illingworth, R. E.: *Quart. J. Exper. Physiol.* 21: 93, 1931. Slotta, K. H., and Ruschig, H.: *Ztschr. f. physiol. Chem.* 228: 207, 1934; *Helv.* 17: 1361, 1934. Slotta, K. H., Ruschig, H., and Fels, E.: *Berichte* 67: 1270, 1934. Slotta, K. H., Ruschig, H., and Blanke, E.: *Berichte* 67: 1947, 1934. Smith, P. E., and Engle, E. T.: *Proc. Soc. Exper. Biol. & Med.* 29: 1225, 1932. Tausk, M., de Fremery, P., and Luchs, A.: *Acta Brevia Neerl.* 1: 4, 1931. Tausk, M., de Fremery, P., Luchs, A., and Reynolds, S. R. M.: *Acta Brevia Neerl.* 4: 85, 1934. Wintersteiner, O., and Allen, W. M.: *J. Biol. Chem.* 107: 321, 1934.

NOTE: In a recent note in *Science* (Vol. 82, No. 2120, page 153), signed by W. M. Allen, A. Butenandt, G. W. Corner and K. H. Slotta, the newly adopted name for the corpus luteum hormone is given as *progesterone*. Heretofore it has been known as *progestin* (Wintersteiner and Allen) and *luteosterone* (Slotta et al.). In this paper the B-type crystals of progestin (on p. 1280) are known now as A *progesterone*, and the C-type crystals of progestin (on p. 120. 5°-121°) are now known as B *progesterone*.

## CANCER OF THE FEMALE URETHRA\*

EUGENE S. AUER, M.D., ST. LOUIS, MO.

(From Gynecological Service of the Bernard Free Skin and Cancer Hospital)

THE relative scarcity of primary carcinoma of the female urethra justifies this report of 22 cases. Counseller and Paterson,<sup>1</sup> reviewing the literature in 1933, found a total of 136 cases, including 12 of their own. Two cases reported by Fukai and Yoshida<sup>2</sup> are not included in their summary. Benson<sup>3</sup> reported a case in 1932. Mereur and Grenier<sup>4</sup> reported a case in 1933, as did Eichenberg<sup>5</sup> and Muller,<sup>6</sup> respectively. Pomeroy<sup>7</sup> reported 3 additional cases in 1934. The 22 cases, which are included in this report, bring the total number of cases found in the literature to 167. Were this figure a true one, carcinoma of the female urethra would indeed be a rarity. However, many times this number of patients probably have been treated, but have gone unreported.

\*Read at a meeting of the St. Louis Gynecological Society, May 10, 1935.

Eighteen of these patients were seen at the Barnard Free Skin and Cancer Hospital, on the services of Drs. G. Gellhorn and F. J. Taussig. The other 4 patients were seen and treated by these 2 men in their private practice. Fifteen cases were seen more than five years ago. The balance were seen during the years from 1930 to 1934. Of the 15 patients seen before 1930, 2 refused treatment, 8 are dead, and 5 survived the five-year period. The 2 patients who refused treatment were not followed by the social service department, so that their fate is unknown. Six of the 7 patients treated within the past five years remain alive and apparently well, periods varying from a few months to almost five years.

The average age of these patients was fifty-four. The youngest was thirty-nine and the oldest seventy-five. This high average age is in accordance with the figures quoted by various other authors. All of these patients were married, but this fact is of academic interest, rather than of significant value, because approximately 95 per cent of all the patients examined in our clinic are or have been married. Ninety-two per cent of all the patients examined have borne children, so that the question of parity in our patients with urethral cancer is of no consequence in relation to etiology. The figures mentioned relate only to white women, as no colored women were seen with urethral cancer. Urethral caruncle has preceded the cancer in several of these cases. It is the only concrete evidence that could possibly be taken as a predisposing factor.

The point of origin for cancer of the female urethra is probably on the posterior wall at or near the external urinary meatus. In practically all of the early cases this was the area involved. In the more advanced cases the posterior urethral wall was always invaded; whereas, the anterior wall sometimes was found free of cancerous invasion. So far as can be ascertained, the middle and posterior third of the urethra have never been the primary site of the neoplasm.

The chief complaint of the patients was pain and burning on urination. Frequency of urination was the next complaint in order of frequency. Practically all of the advanced cases gave one of these symptoms as their earliest complaint, although at the time that they presented themselves for examination, other symptoms, such as bleeding, swelling, or local growth were noted. There was one case of acute urinary retention prior to treatment.

In this series there was a great predominance of squamous cell carcinoma. There was one primary melanoma and two adenocarcinomas. The former is an extremely rare lesion, only three or four having previously been reported. However, Dr. Q. U. Newell<sup>8</sup> of this city, treated another woman with melanoma of the urethra at about this same time. His patient is still alive about two and a half years after treatment. A complete report of this extremely rare lesion and a review of the literature will soon be made available by him.



Treatment of these cases has consisted of local excision or local radiation, with small, well-screened doses of radium. Radium is best used in the form of emanations, in either gold or platinum seeds. If this form of radiation is unavailable, 25 to 50 mg. of radium element, screened in the equivalent of 1.25 mm. of platinum, surrounded by rubber sewed into the urethral canal at the site of the lesion, should be used. We have employed from 400 mg. hours to 4,100 mg. hours in the local treatment of urethral carcinoma, the amount depending entirely on the size of the local lesion. No arbitrary dosage of radium can be prescribed, as radium dosage is entirely a matter of experience. Despite the large amount of tissue damage resulting from some of the radiation, only two patients had incontinence of urine.

In certain instances radical surgical removal of the regional lymphatics, both above and below the inguinal ligament (Basset operation)<sup>9</sup> was done in addition or in combination with the local treatment. X-ray therapy was used as a palliative measure in three cases. We do not believe that x-ray therapy is efficacious in the treatment of the local lesion, or of glandular metastases. Therefore, it was not used as a therapeutic agent.

The age and physical condition of the patient, the extent of the local lesion, and the presence of palpable inguinal glands were factors in the decision as to the method of choice in the treatment of any individual case. Every cancer patient, regardless of the location of the lesion, must be considered individually, and no single treatment should be advocated to cover a group of patients with the same lesion. In this series of cases no patient of extreme age was subjected to a radical surgical procedure. Neither was this operation used in patients who were obviously in a hopeless condition. Therefore, only early and moderately advanced cases were primarily considered as being suitable for radical surgery in addition to local treatment of the urethral cancer.

The Basset operation is a comparatively safe surgical procedure. The operative mortality is low when the patient's general condition is good. The lymphatic drainage of the female urethra is similar to that of the vulva, and this same operation has produced excellent results in the hands of Taussig<sup>10</sup> who has reported 63 per cent five-year cures in a large series of vulvar carcinoma. Six Basset operations were performed in this series of cases with no mortality. Neither has there been a recurrence of cancer in any of these patients. In one case, the melanoma, it was impossible to clear up the local condition, and metastases to the bladder and other parts of the body caused death in one year.

We now believe that the Basset operation, combined with local radiation, is the treatment of choice in all early and moderately advanced cases of cancer of the female urethra, if in the judgment of the operator the patient is a fairly good operative risk. The small size of a local lesion that has proved to be cancer by microscopic examination should never

influence one toward conservatism in the treatment of this condition, for metastases have been found in the regional lymph nodes with an extremely small primary lesion. Conversely only hyperplastic nodes have been found with relatively far-advanced local lesions. It seems quite evident that carcinoma of apparently the same type and grade metastasizes in different individuals differently according to some unknown characteristic. We agree with Mikulicz<sup>11</sup> in his belief that a third of all cases of cancer with this same lymphatic drainage have regional lymphatic metastases. It is only by operation that these patients with glandular metastases have a chance of ultimate survival. In our hands the use of x-ray on lymphatic metastases has been very disappointing, if not entirely without merit.

TABLE I

TREATMENT	NUMBER	DIED	CURES LIVED MORE THAN 5 YEARS	LIVING AND WELL LESS THAN 5 YEARS
Local, only	14	8	2	4
Local plus Basset operation	6	1	3	2
No treatment	2	2	0	0
Total	22	11	5	6

*Summarizing the Results of Treatment:* Nine early cases were seen. Two patients refused treatment. Six had only local treatment, and one had local treatment plus a Basset operation. Two of the three early cases treated more than five years ago lived more than five years. The third died of metastases four years after local excision. This case emphasizes the necessity for gland removal in the earliest cases. Of the four more recent cases, one had a cautery excision more than three years ago. Two had cautery excision followed by less than 900 mg. hours of heavily screened radium almost five years and one year ago, respectively. The fourth had radium locally followed by a Basset operation. All of these women are living and apparently free of cancer at the present time.

Five advanced cases have been treated. One patient had radium locally and is alive and well more than two years. The other four had a Basset operation in addition to local destruction of the tumor by means of cautery or radium. One is well more than two years, one is well more than five years, one is alive more than twelve years, and the fourth patient died nine years after treatment, due to cancer of the breast, which was considered a new malignancy and not a metastatic growth.

The remaining eight patients were considered hopeless when seen. All were given palliative radiation, except one, who had a Basset operation in addition to local radiation, because of the highly malignant nature of the tumor, and with the hope that her life could possibly be prolonged. She lived one year after treatment; whereas, none of the others survived a six-month period.

The results of treatment in this small series of cases make certain conclusions logical. First, except in very far-advanced cases that are considered hopeless when seen, the prognosis is good. This is in contradiction to almost all other authors on this subject. Second, the early case of urethral cancer in the female can be successfully treated by local excision, local radiation, radical surgery, or a combination of either of the first two with the third. We strongly urge the routine use of the Basset operation in combination with local radiation as the method of choice in these early cases, as even the very early case may have already metastasized to the regional lymphatics in spite of the minuteness of the visible lesion. Third, the advanced case that is not yet hopeless is best treated by local radiation and Basset operation, as practically all of these cases will show glandular metastases. Fourth, the very far-advanced case that is practically hopeless when first seen should receive only palliative treatment and as much relief from terminal pain as is possible.

## REFERENCES

- (1) Counseller, V. S., and Paterson, S. J.: *J. Urol.* 29: 587, 1933. (2) Fukai, A., and Yoshida, S.: *Acta Dermatol.* 9: 239, 1927. (3) Benson, H. W.: *Chicago M. Rec.* 54: 70, 1932. (4) Mercur, O., and Grenier, E. P.: *J. de l'Hôtel-Dieu de Montreal* 2: 241, 1933. (5) Eichenberg, H.: *Ztschr. f. Geburtsh. u. Gynäk.* 105: 505, 1933. (6) Muller, C.: *Ztschr. f. Geburtsh. u. Gynäk.* 105: 462, 1933. (7) Pomeroy, L. A.: *AM. J. OBST. & GYNEC.* 27: 606, 1934. (8) Newell, Q. U.: Personal Communication. (9) Taussig, F. J.: In Curtis, A. H., *Obstetrics & Gynecology*, Philadelphia, 1933, W. B. Saunders Co. (10) Taussig, F. J.: *Surg. Gynec. Obst.* 60: 477, 1935. (11) von Mikulicz-Radecki, F.: *Zentralbl. f. Gynäk.* 55: 2922, 1931.

1045 MISSOURI THEATER BUILDING

---

Rose, D. K.: Postpartum Pyelitis of Pregnancy, *Am. J. Surg.* 25: 394, 1934.

In postpartum pyelonephritis with bladder retention in which catheter interference is indicated either from dysuria or toxicity, two entirely opposite types of bladder function are encountered. Either may exist separately, or the two may coexist to any degree.

The postpartum bladder showing a relatively fixed, compensated bladder wall back of a physiologic block of the external sphincter, if of sufficient degree, requires continuous drainage when indicated by reason of infection. Such drainage primarily reduces bladder infection and, secondarily, urethral, pelvic and kidney infection by facilitating ureteral flow by a decompressed and perfectly drained bladder. Intermittent catheterization in such a bladder traumatizes in the presence of imperfect drainage and tends to generalize the infection. Irritative instillations in such bladders are contraindicated.

If sufficient degree of altered bladder function occurs, continuous bladder drainage is indicated until perfect function is restored.

The postoperative bladder with inhibited or functionally weakened bladder wall and with normal sphincter tone requires only intermittent catheterization. Irritating instillations in these bladders may be of value.

J. THORNWELL WITHERSPOON.

## BLOOD LIPIDS IN ECLAMPSIA

ELDON M. BOYD, M.A., M.D., C.M., ROCHESTER, N. Y.

(From the Department of Obstetrics and Gynecology, the University of Rochester, School of Medicine and Dentistry)

**B**LOOD lipids have been determined in eclampsia on several occasions. Cholesterol, being the most readily estimated, has received the greatest amount of attention. Serum cholesterol was reported in three cases of eclampsia in 1911 by Chauffard, Laroche and Grigaut<sup>13</sup> who found no consistent variation from the concentration in the serum of healthy gravidas. A similar conclusion may be drawn from a collective survey of subsequent work on blood cholesterol.<sup>1, 12, 14, 17, 21, 23</sup>

A differential analysis of all or nearly all of the blood lipids in eclampsia has been made in whole blood by Lindemann<sup>18</sup> and by Slemons and Stander<sup>24</sup> and on serum by Hellmuth.<sup>16</sup> Lindemann<sup>18</sup> has presented the largest series of cases and his results, although determined over twenty years ago with a less refined technic than is possible now, bear many points of similarity to those recorded below. He concluded that blood lipoids were elevated in eclampsia and the "fat" low; analysis of his results reveals that he got an increase in the phospholipid to cholesterol ratio. Slemons and Stander<sup>24</sup> concluded that there was no significant change in the concentration of any lipid in whole blood but again four of their six cases may be seen to have had a phospholipid cholesterol ratio higher than their average for normal pregnancy. Hellmuth<sup>16</sup> reported four cases, none showing any marked changes in serum lipids.

It became obvious to the author that if any variation in the blood lipids were to be found in eclampsia, a correlative study of all the lipids in whole blood, plasma and the red blood cells would be required. This principle was apparent in a survey of blood lipids in normal gestation, in which Boyd<sup>6</sup> found that the major changes occurred in plasma only and affected to different degrees the values of the several lipids. The nature and concentration of the lipids of plasma differ from those of the red blood cells and whole blood analyses are in general unsatisfactory, a fact also emphasized by Boyd in a study of the blood lipids in relation to lactation<sup>9</sup> and to fever.<sup>10</sup>

The patients studied were from the Obstetrical Divisions of the Strong Memorial Hospital. When possible, blood was obtained with the patient in a fasting state; when a patient was in convulsions, blood was taken irrespectively of whether or not the patient had ingested food within fifteen hours. Recent work<sup>8</sup> has cast doubt on the popular opinion that blood lipids are markedly increased in value after meals,

at least in normal persons. The lipid composition of whole blood, plasma and the red blood cells was determined by Bloor oxidative micromethods as modified by Boyd.<sup>3, 4, 8</sup> The lipid content of the white blood cells was likewise determined but found to be no different from that of healthy gravidas<sup>7</sup> and of nonpregnant women;<sup>5</sup> hence these results have not been reported.

#### CHANGES IN BLOOD PLASMA

As in normal gestation, so in eclampsia the most significant changes in blood lipids occurred in plasma, the results of which are given in Table I. In this table are included values for plasma lipids in five cases of eclampsia and two cases of preeclampsia which exhibited variations similar to those found in the eclamptic cases. These latter two cases have been considered to be cases of "eclampsia without convulsions" or to belong to what has been termed the "eclamptic state." The author has examined blood from many cases of so-called preeclampsia, but only two exhibited the same changes as the convulsive patients, these being the two included in Table I. Changes in the blood lipids in the remaining nonconvulsive or "noneclamptic"

TABLE I. THE LIPID COMPOSITION OF BLOOD PLASMA IN THE ECLAMPTIC STATE. THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF PLASMA

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					RATIO P/TO
		NEU- TRAL FAT	CHOLESTEROL			PHOS- PHO- LIPID	
			TOTAL	ESTER	FREE		
Preeclampsia	1032	309	256	172	84	352	1.38
Preeclampsia	1350	382	321	205	116	510	1.59
Intercurrent eclampsia	513	101	138	90	48	214	1.55
Antepartum eclampsia	991	408	191	118	73	314	1.64
Antepartum eclampsia	806	276	193	86	107	279	1.45
Antepartum eclampsia	987	528	138	92	46	259	1.88
Postpartum eclampsia	1445	572	277	161	116	488	1.76
Mean of eclamptic state	1018	368	216	132	84	345	1.61
Standard deviation	292	147	65	44	28	106	0.16
Standard deviation in per cent of mean	29%	40%	32%	33%	33%	31%	10%
Normal pregnancy	900	353	205	140	65	248	1.22
Mean $\pm$ St. Dev.	$\pm 130$	$\pm 75$	$\pm 45$	$\pm 47$	$\pm 15$	$\pm 43$	$\pm 0.12$
Nonconvulsive pre- eclampsia	863	275	233	160	73	250	1.08
Mean $\pm$ St. Dev.	$\pm 119$	$\pm 117$	$\pm 24$	$\pm 27$	$\pm 12$	$\pm 27$	$\pm 0.10$

preeclamptic patients have been found<sup>12</sup> to be entirely different from the changes in the convulsive group. For comparative purposes, means for this group and for normal pregnancy as found in previous investigations<sup>6, 11</sup> have been included in Table I and, as indicated, in the remaining tables.

The mean value of each lipid was determined and the standard deviation of the mean calculated from the formula

$$\theta = \sqrt{\Sigma(x)^2/n}$$

where  $\theta$  represents the standard deviation,  $\Sigma$  a summation symbol,  $x$  the variation of each value from the mean and  $n$  the total number of readings. The means and standard deviations so obtained have been compared with corresponding values deduced for normal pregnancy<sup>6</sup> and the nonconvulsive toxemias of pregnancy.<sup>11</sup> Statistically, the difference between two groups of values may be considered significant when the mean plus or minus the standard deviation for one group is beyond the mean plus or minus the standard deviation for the other group. This indicates that two-thirds of all values in the one group may be expected to be beyond two-thirds of all values of the second group. The mean plus or minus twice the standard deviation includes 95 per cent of all expected values for the group. The results have been submitted to this critical survey because all too frequently significant differences have been claimed on variation of means alone, which is quite inadequate.

The point is well illustrated in the present figures. Thus, the mean values of all lipids except ester cholesterol were higher in eclampsia than in normal pregnancy. Offhand one might conclude, as did Lindemann,<sup>18</sup> that the concentration of lipids is increased in eclampsia. The standard deviations reveal that the range for eclampsia was greater than that for, and included the range of, normal pregnancy. Hence it may be concluded that there is no significant variation in the concentration of any lipid of plasma in eclampsia.

When, however, the difference between the ratio, phospholipid/total cholesterol (P/TC) is considered, a significant variation may be noted. The mean value for the ratio was 1.22 in normal pregnancy, 1.08 in the nonconvulsive toxemias and 1.61 in eclampsia. The range, mean  $\pm \theta$ , for eclampsia was well above the same range for normal gestation and for the nonconvulsive toxemias. Statistically it may be concluded that three-fourths of all values for the ratio in eclampsia will be above three-fourths of all values for the ratio in noneclamptic patients. Actually, the author has never found a value for the P/TC ratio above 1.40 in noneclamptic toxemias or in normal gravidas except in the two cases of preeclampsia which have been included in Table I. Both of these cases exhibited muscular twitchings in addition to the usual symptoms of preeclampsia and in view of the lipid findings, they have been grouped as literally preclamptic.

Further evidence that the increased P/TC ratio in eclampsia is significant may be deduced from the percentage standard deviations ( $\theta/\text{mean} \times 100$ ) given in Table I. The percentage standard deviation

for the plasma lipids varied between 29 and 40 per cent. The percentage standard deviation for the P/TC ratio was 10 per cent. This indicates that the variation of the P/TC ratio from one case to another was only one-third or one-quarter the variation in single lipid values. In other words, although the concentration of plasma lipids varies greatly in eclampsia, a fact noted by previous authors, the ratio P/TC is consistently and regularly high.

The author believes, therefore, that a high plasma P/TC ratio may be said to characterize the eclamptic state. He has tentatively selected a ratio of 1.40 as the dividing line between eclamptic and noneclamptic cases. This value may require a slight shift up or down in the light of subsequent work. The value depends also, of course, on the use of methods exactly as herein given.

#### CHANGES IN WHOLE BLOOD

In Table II have been given the means and standard deviation of the lipid values for whole blood in eclampsia. A survey of the values will reveal that in each case the range in eclampsia overlaps considerably

TABLE II. ILLUSTRATING THAT THE SIGNIFICANT CHANGES ENCOUNTERED IN PLASMA DO NOT APPEAR IN WHOLE BLOOD. RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF WHOLE BLOOD

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					RATIO P/TC
		NEU- TRAL FAT	CHOLESTEROL			PHOS- PHO- LIPID	
			TOTAL	ESTER	FREE		
Mean of eclamptic state	829	219	187	90	97	361	1.96
Standard deviation	255	120	56	39	22	102	0.29
Normal pregnancy	785	248	179	95	84	293	1.66
Mean $\pm$ St. Dev.	$\pm 117$	$\pm 63$	$\pm 35$	$\pm 29$	$\pm 11$	$\pm 52$	$\pm 0.26$

the range for normal pregnancy. A similar overlapping occurred with the P/TC ratio of whole blood. Hence it may be concluded that the significant changes encountered in plasma do not appear in whole blood. The previous studies of Lindemann<sup>18</sup> and of Slemons and Stander<sup>24</sup> were with whole blood.

#### CHANGES IN THE RED BLOOD CELLS

The lipid composition of the red blood cells in eclampsia likewise was found to exhibit no significant variation from that in normal pregnancy (Table III). The noneclamptic toxemias were distinguished from the eclamptic by having considerably more neutral fat in the red blood cells. Boyd<sup>11</sup> has shown that the characteristic of these non-convulsive toxemias is an alteration of the normal equilibrium between the lipids of plasma and those of the red blood cells.

## RECOVERY FROM ECLAMPSIA AND THE PLASMA P/TC RATIO

From the above survey of the lipid concentration in whole blood, plasma and the red blood cells, it was concluded that one change and one alone characterized the blood lipids in the eclamptic state, i.e., an increase in the plasma P/TC ratio. Further proof that this alteration is significant may be seen in the return to normal of the plasma P/TC ratio when the patients recovered from eclampsia. In four cases of eclampsia, the author was enabled to take samples of blood on several occasions during convulsions and recovery. Variations thus found in the plasma P/TC ratio are given in Table IV. It may be seen that as the patient improved and then recovered from the convulsive state, the ratio fell from its high value to 1.0 or lower, which is about normal. This again is evidence that the eclamptic state is associated with a high plasma P/TC ratio.

TABLE III. THE LIPID CONTENT OF THE RED BLOOD CELLS IN THE ECLAMPTIC STATE. THE RESULTS ARE EXPRESSED IN MG. PER 100 C.O. OF CELLS

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID				
		NEU-TRAL FAT	CHOLESTEROL			PHOSPHO-LIPID
			TOTAL	ESTER	FREE	
Mean of eclamptic state	638	78	146	40	106	387
Standard deviation	333	63	88	58	29	196
Normal pregnancy	594	89	133	16	121	361
Mean $\pm$ St. Dev.	$\pm 123$	$\pm 80$	$\pm 62$	$\pm 21$	$\pm 43$	$\pm 155$
Nonconvulsive pre-eclampsia	826	246	131	7	125	458
Mean $\pm$ St. Dev.	$\pm 128$	$\pm 101$	$\pm 21$	$\pm 8$	$\pm 17$	$\pm 59$

TABLE IV. ILLUSTRATING THAT THE ELEVATED P/TC RATIO IN THE ECLAMPTIC STATE DISAPPEARS AS THE PATIENT RECOVERS

PATIENT	DAY OF DISEASE	CLINICAL CONDITION	P/TO RATIO
R. F.	16 days antepartum	Convulsions	1.55
	9 days antepartum	No convulsions, patient apparently well	1.98
	2 days antepartum	Return of all symptoms but no convulsions; labor induced	
	1 day postpartum	Patient rapidly recovering	1.37
R. W.	1 day antepartum	Convulsions	1.64
	2 days postpartum	Improving	0.94
	9 days postpartum	Recovered	0.69
M. S.	2 days antepartum	Convulsions	1.45
	1½ days postpartum	Improving	1.24
	6 days postpartum	Recovered	1.04
	11 days postpartum	Recovered	1.13
M. W.	1 hour postpartum	Convulsions	1.76
	12 hours postpartum	Convulsions ceased	1.41
	14 days postpartum	Recovered	1.13

## THE RELATION OF THE PLASMA P/TC RATIO TO CONVULSIONS

In one case of intercurrent eclampsia, patient R. F. in Table IV, lipid analyses revealed that a high ratio may be present without convul-



sions necessarily occurring. This patient had convulsions shortly after admission to hospital and at that time gave a plasma P/TC ratio of 1.55. Under a modified Stroganoff treatment she recovered and most of her symptoms disappeared. A week after the initial convulsions, lipid analysis revealed an even higher ratio, 1.98. One week later again, all her symptoms (hypertension, albuminuria, edema, etc.) suddenly returned but no convulsions occurred. Labor was induced and the patient delivered. In the second day of the puerperium she began to improve rapidly and her ratio fell immediately to 1.37. This

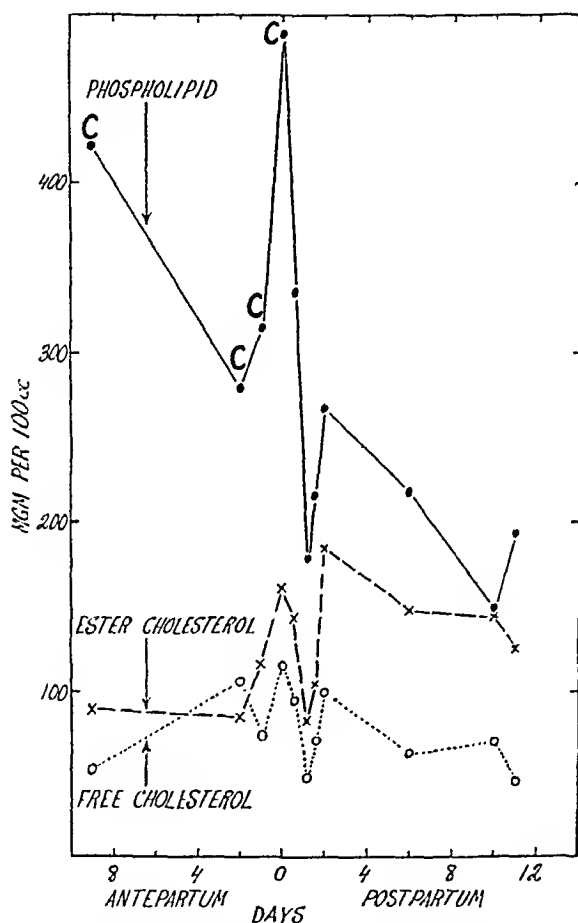


Fig. 1.—The values of plasma phospholipid, ester cholesterol and free cholesterol in relation to convulsions in, and recovery from, eclampsia. The presence of convulsions is indicated by a C.

suggests that the high ratio is not due to convulsions but to the underlying cause of the eclamptic state. The case also exhibited the value of estimating the ratio in determining the course of action to be taken in dealing with such types of eclampsia.

#### TO WHAT IS THE ELEVATED PLASMA P/TC RATIO DUE?

An elevation of the plasma P/TC ratio may be due to two things, (a) an increase in phospholipid or (b) a decrease in total cholesterol. The data given in Table I indicate that either one or both of these factors

may operate to increase the ratio in eclampsia. Study of the plasma lipids during recovery from eclampsia suggested that a return to normal in the ratio is due chiefly to a decrease in the concentration of phospholipid.

The puerperium of eclamptic patients was found associated with a fall in the value of plasma neutral fat and phospholipid; minor changes occurred in the cholesterol fractions and in fact ester cholesterol actually rose in value in several instances. No relation has been noted between neutral fat and eclampsia and the decreasing value of this lipid in the puerperium corresponded to the decrease found during lactation in normal puerperas.<sup>9</sup> These changes have been shown graphically in Fig. 1.

In Fig. 1 there have been plotted the values for phospholipid and both cholesterol fractions, i.e., the lipids directly concerned in determining the value of the P/TC ratio. It may be seen that when the ratio returns to normal, the change is due chiefly to a decrease in the concentration of phospholipid, no change in free cholesterol and perhaps a slight increase in ester cholesterol.

#### SIGNIFICANCE OF THE P/TC RATIO

Mayer and his associates, especially Schaeffer and Terroine, proposed some years ago that lipid ratios (in tissues) were equally if not more important than the actual concentration of single lipids. In recent years the tendency has been to discount the importance of the lipid ratios and return to actual lipid values. From time to time, however, reports have appeared which showed that perhaps there was some significance in the ratios. Thus, McQuarrie, Bloor, Husted and Patterson<sup>19</sup> found comparatively minor changes in the lipid composition of blood plasma of 100 epileptic children, but McQuarrie, Husted and Bloor<sup>20</sup> subsequently showed that a significant increase in the plasma P/TC ratio occurred at or about the time of convulsions in epilepsy. Two deductions may be made from this work which are of importance to the interpretation of the present data. First, the changes in the plasma P/TC ratio were found more significant than changes in the individual lipid values, exactly as herein found, and second, the plasma P/TC ratio was found highest at the time of the epileptic convulsions. Clinically the sequence of the convulsion in grand mal is almost identical with that in eclampsia. It appears probable that a similar change in body metabolism is responsible for both convulsions. This change is characterized by, and may even be due to, an elevated plasma P/TC ratio.

Considerable has been written on the antagonism between phospholipid and cholesterol, and Sinclair<sup>22</sup> has presented a recent able review of the subject. Briefly, under normal conditions the relation between phospholipid and cholesterol both in blood and in tissues is fairly con-

stant: when one increases the other increases and vice versa. Phospholipid is hydrophilic and cholesterol is hydrophobic. Intravenous injections of large amounts of an emulsion of phospholipids increase the value of blood phospholipid and favor the retention of water by the tissues. A relative increase in blood phospholipid is apparently, therefore, accompanied by a relative increase in tissue phospholipid, thus favoring the retention of water in the tissues.

In the eclamptic state, a somewhat similar situation may be deduced from the present results. There has been shown to occur a relative increase in plasma phospholipid. It may be offered that probably this altered equilibrium between blood and tissues would result in a relative increase in tissue phospholipid, thus favoring retention of water by the tissues. There is a good deal of evidence suggesting a change of water balance in eclampsia. Clinically, the patients have a noticeably puffy appearance. Harding and Van Wyck<sup>15</sup> found that administration of sodium chloride, which also favors retention of water in the tissues, increased all the symptoms of toxic pregnancy.

The relation of water retention to convulsions becomes more apparent if attention is confined to the tissues of the brain. Increased water retention by the brain, due, may it be offered, to an increased plasma P/TC ratio favoring increased phospholipid values in the brain, will result in increased pressure within the bony skull. When this surpasses a certain maximum, the irritability of the nerves may reach a point at which convulsions ensue. Such an explanation, deduced from the present data, is offered as a working hypothesis, not as a proved theory.

#### METHOD FOR DETERMINING THE PLASMA P/TC RATIO

Add 2 c.c. of plasma to 35 to 40 c.c. of alcohol ether (3:1, both redistilled), heat to boiling for two minutes on a steam bath, cool, filter through alcohol-extracted filter paper, wash with solvent, press out the precipitate, and make filtrate up to 50 c.c.

(a) *Phospholipid*: 25 c.c. of the alcohol ether extract are evaporated to dryness without overheating in tall 100 c.c. beakers. Add 2 or 3 c.c. of redistilled petroleum ether, heat to boiling, and pour off into a 15 c.c. centrifuge tube. Repeat extraction 5 times. Centrifuge. Pour supernatant solution quantitatively into 15 c.c. graduated centrifuge tube and evaporate to just below 1 c.c. Make up to 1 c.c. with petroleum ether, add 7 c.c. of dried, redistilled acetone and 0.1 c.c. of 30 per cent magnesium chloride in 95 per cent alcohol. Let stand one-half hour. Centrifuge, pour off supernatant solution and discard it (or by evaporating it and redissolving in alcohol it may be used for total cholesterol if the amount of blood is limited, in which case 1 c.c. of plasma will suffice). Dry with air and dissolve precipitate of phospholipids in 10 c.c. of moist ether with stirring. Centrifuge and transfer quantitatively to a 125 c.c. glass-stoppered Erlenmeyer flask. Evaporate off solvent and avoid overheating; remove last traces of ether vapor with a gentle stream of air. Add 3 c.c. of Nieloux reagent (prepared after Bloor<sup>2</sup>), and 5 c.c. of 1 N potassium dichromate. Heat for twenty minutes at  $124 \pm 2^\circ$  C. in an oven, placing flask on a cast iron plate. Remove from oven, add 75 c.c. of ice cold distilled water,

10 c.c. of 10 per cent potassium iodide and titrate with 0.1 N sodium thiosulphate, using 1 per cent starch solution as an indicator. Subtract the value obtained from that of a blank containing only the oxidizing agents and heated as the unknown, divide the difference by 3 and multiply by 100 which gives the mg. of phospholipid per 100 c.c. of plasma. All glassware must be cleaned with chromic acid cleaning solution, thoroughly rinsed with distilled water and dried. All the solvents must be redistilled and free of organic matter, the ether being also peroxide free.

(b) *Total Cholesterol*: The author has recently described the method for the microestimation of total cholesterol using digitonin precipitation followed by oxidation as with phospholipid<sup>4</sup> to which may be added certain precautions and minor modifications later found.<sup>8</sup> By these procedures the concentration of total cholesterol in milligram per cent is found. The value of the phospholipid total cholesterol ratio is then found by dividing the phospholipid value by that for total cholesterol. For further details of method, previous papers by the author may be referred to<sup>3, 6, 7, 8</sup> as well as references to the work of Bloor, Okey, Yasuda, etc., therein contained.

#### SUMMARY

In order to ascertain if there were any *significant* changes in the blood lipids in eclampsia, a quantitative estimation of *all* lipids in whole blood, plasma, the red blood cells and the white blood cells was made. It was found that the concentration of lipids varied greatly in eclamptic patients but no significant variation occurred in the value of any *single* lipid.

The ratio of phospholipid to cholesterol in plasma was found, however, to be without exception higher in eclampsia than in other toxemias or in normal gestation. The mean minus the standard deviation for the ratio in eclampsia was higher than the mean plus the standard deviation in normal gravidas and other toxemias. Variations in the value of the ratio from one eclamptic patient to another were only one-third to one-fourth as great as the variation in single lipids, indicating that the ratio was also less variable than the component lipids.

When the patients recovered from eclampsia, the ratio P/TC of plasma returned quickly to normal due chiefly to a fall in the value of phospholipid.

Cessation of convulsions without termination of pregnancy left the ratio still high, indicating that a high ratio did not result from convulsions but was associated with and possibly accounted for the eclamptic state.

Only a small proportion of cases diagnosed as preeclampsia were found to have an elevated plasma P/TC ratio and, hence, were literally preeclamptic. The test is at present being used as a means of separating the preeclamptic group into true preeclampsia and non-convulsive cases.

A possible relationship between the elevated ratio and water balance in connection with the etiology of eclampsia has been given.

The method of estimating the plasma P/TC ratio has been outlined and the clinical value of the same briefly indicated.

NOTE: The author wishes to express his appreciation of cooperation given by various members of the staff of the Department of Obstetrics and Gynecology of the Strong Memorial Hospital, Rochester, New York.

The major portion of this work was done at Rochester, New York. Two cases were added to the list from the Nicol Wing of the Kingston General Hospital, Kingston, Ontario, Canada.

#### REFERENCES

- (1) *Autenreith, W., and Funk, A.*: München. med. Wehnschr. 60: 1243, 1913.
- (2) *Bloor, W. R.*: J. Biol. Chem. 82: 273, 1929. (3) *Boyd, E. M.*: J. Biol. Chem. 91: 1, 1931. (4) *Idem.*: J. Biol. Chem. 101: 323, 1933. (5) *Idem.*: J. Biol. Chem. 101: 623, 1933. (6) *Idem.*: J. Clin. Investigation 13: 347, 1934. (7) *Idem.*: Surg. Gynec. Obst. 59: 744, 1934. (8) *Idem.*: J. Biol. Chem. 110: 61, 1935. (9) *Idem.*: AM. J. OBST. & GYNEC. 29: 797, 1935. (10) *Idem.*: Canadian Med. Assn. J. 32: 500, 1935. (11) *Idem.*: Unpublished data. (12) *Bürger, M., and Beumer.*: Berl. klin. Wehnschr. 50: 112, 1913. (13) *Chauffard, A., Laroche, G., and Grigaut, A.*: L'Obstetrique 4: 481, 1911. (14) *Dieckmann, W. J., and Wegner, C. R.*: AM. J. OBST. & GYNEC. 23: 657, 1932. (15) *Harding, V. J., and Van Wyck, K. B.*: AM. J. OBST. & GYNEC. 24: 820, 1932. (16) *Hellmuth, K.*: Arch. f. Gynäk. 127: 293, 1926. (17) *Huffmann, M.*: Centralbl. f. Gynäk. 39: 33, 1915. (18) *Lindemann, W.*: Ztschr. f. Geburtsh. u. Gynäk. 74: 819, 1913. (19) *McQuarrie, I., Bloor, W. R., Husted, C., and Patterson, H. A.*: J. Clin. Investigation 12: 247, 1933. (20) *McQuarrie, I., Husted, C., and Bloor, W. R.*: J. Clin. Investigation 12: 255, 1933. (21) *Schlimpert and Huffmann, M.*: Deutsche med. Wehnschr. 39: 583, 1913. (22) *Sinclair, R. G.*: Physiol. Rev. 14: 351, 1934. (23) *Stemons, J. M., and Curtis, C. S.*: Am. J. Obst. 75: 569, 1917. (24) *Stemons, J. M., and Stander, H. J.*: Johns Hopkins Hosp. Bull. 34: 7, 1923.

QUEENS UNIVERSITY, KINGSTON, CANADA

## TRIBROMETHYNOL PREMEDICATION IN OPERATIVE GYNECOLOGY

JAMES L. REYCRAFT, M.A., M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, Western Reserve University and Lakeside Hospital)

THE gynecologist, as well as the general surgeon, now has at his disposal an extensive array of agents which can be used in the preparation of his patients for operation. For many years the usual preparation of gynecologic patients, other than local, has been the administration of a hypodermic of morphine and atropine. Twenty years ago or more, scopolamine was added in certain instances to develop the state of amnesia which was desirable in operating in certain cases. This did not lend itself to use in gynecology and hence did not become popular. During the same period there was a gradual tendency to get away from the use of deep anesthesia with ether, and nitrous oxide and ethylene with or without local infiltration were utilized.

In the past decade a refinement in preparation has appeared in that various premedications have become available, especially the numerous barbiturates. Dial, pentobarbital sodium, phenobarbital, and sodium amytal are most commonly used. Some of these may be given intra-

venously and rectally, as well as orally, and are at times valuable. In our opinion, however, they are most efficacious when administered after operation.

The first mention of tribromethynol (avertin) was by Eiehholtz<sup>1</sup> in 1924 as a rectal anesthetic. It is tribromethylalcohol, and its chemical formula is  $\text{CBr}_3 \text{CH}_2\text{OH} \xrightarrow{-\text{HBr}} \text{CBr}_2 = \text{CHOH} \rightarrow \text{CBr}_2\text{HCHO}$ .

Dosage tables have been formulated showing the amount of avertin fluid and properly warmed distilled water required for a 2.5 per cent solution. It is important that distilled water be used to prevent unfavorable chemical reactions.

It is not the purpose of this paper to discuss the technique of the administration of this product; we merely state that it is given as a rectal instillation approximately one-half hour before the patient is taken to the operating room. An enema is given the night before, but none at the time of administration. It is customary to give morphine  $\frac{1}{6}$  gr. with or without atropine just before the patient is taken to the operating room.

#### DOSAGE

In the early days of the use of avertin it was recommended for actual surgical anesthesia. This was accomplished by giving large doses, even as much as 120 or 140 mg. per kilogram of body weight. Experience has taught that it has no place in this field but should be employed purely as a method of premedication to be followed by the use of local or, more commonly, general anesthesia. The amount used within safe limits, in our estimation, is between 60 and 80 mg. per kilogram of body weight.

#### VARIATIONS IN DOSAGE

A healthy young woman of average weight will take 70 mg. per kilogram, sometimes more. However, the weak, emaciated, dehydrated, or excessively obese patient should not be given more than a 50 or 60 mg. dose.

Tribromethynol is absolutely contraindicated in the presence of severe organic disease of the liver, severe bilateral disease of the kidneys, acidosis, and starvation.

#### ADVANTAGES

The patient usually goes to sleep with little or no excitation and frequently continues to sleep lightly after the operation for several hours; it seems to dull her pain sense much longer than ether or nitrous oxide with the result that her reactions are slower in returning. Many patients never know they were operated upon until many hours later, and all apprehension disappears.

Observers have noted that there is not as much postoperative nausea as when other agents are used; it was found that, if no ether is given,

nausea and vomiting is a postoperative complication in no more than 25 per cent of the cases (White<sup>2</sup>).

There is frequently a state of amnesia, even though the narcosis has been very light, so that the patient has no recollection of anything that happened from the time the drug was administered, even though she was never deeply asleep. In some instances this may carry over for a period of a day or more from the actual time of the operation.

The respirations are quiet, and the drug can be given safely in the presence of cardiac and pulmonary complications. Furthermore, post-operative gas pains are diminished because less ether is required. Since there is very little perspiration during the operation, there is a conservation of body heat.

#### PHARMACOLOGY

Many pharmacologic experiments have been made showing the effects of avertin upon various organs of the body. It is known to be excreted almost entirely through the kidneys although a small amount may pass off through the lungs. Experiments<sup>3</sup> have shown that repeated administration of avertin in very large doses produces a mild parenchymatous degeneration of the liver and kidneys. Shipley and Karns<sup>4</sup> proved it has no irritating effect upon the wall of the bowel. Field and Pileher<sup>5</sup> observed that there was usually a decrease in the urinary output during the first two or three days postoperative but not more marked than in controlled cases with similar operations.

#### COMPLICATIONS

The most startling complication encountered is the lowering of the blood pressure. This may be of serious moment and is the chief reason why avertin is not popular in obstetrics. Furthermore, the drop is exceptionally great in hypertension and the drug should be given very carefully in such cases.

The other complication besides the blood pressure fall which is to be feared is the effect on the respiratory center. The respirations may become extremely shallow, and, if too much opiate has been used, artificial respiration has sometimes been required.

Only last year Barlow<sup>6</sup> advocated the use of sodium pentobarbital for preanesthetic medication, stating that in a series of 1,831 unselected cases from the Lakeside Hospital there was a 30 per cent incidence of postoperative albuminuria in patients receiving avertin, and found a 10 per cent incidence of shock reactions during or after the operation. This has not been borne out in our cases, unless one called every temporary drop of blood pressure a definite evidence of shock, i.e., we have not made the same interpretation of the findings.

A study was undertaken to determine the results in the use of avertin as a premedication or basal anesthetic. We concluded that its use prior

to 1930 was not of sufficient volume to be included. Therefore, all gynecologic patients operated upon by the visiting and associate gynecologic and surgical staffs during 1930, 1931, 1932, 1933, and 1934 were investigated to see if there were evidences of any advantages not found in patients operated upon without its use.

TABLE I. SUMMARY OF OPERATIONS

		NO.	NAUSEA	VOMITING	NEITHER	PER CENT
<i>Major Operations</i>						
Avertin	90 mg.	163	59	32	104	64
Avertin	80 mg.	115	52	32	71	61
Avertin	70 mg.	118	59	34	59	50
Avertin	60 mg.	47	20	14	27	57
Avertin + sodium amytal		22	8	5	14	64
Total		465	198	117	275	59.5
<i>Minor Operations</i>						
Avertin + N <sub>2</sub> O-Oxygen		69	26	12	43	62
Avertin + N <sub>2</sub> O-Oxygen-Ether		30	14	9	16	53
Total		99	40	21	59	58
Total Number of Cases						564

TABLE II. TIME CONSUMED IN 429 MAJOR OPERATIONS

	60" OR LESS	60-80"	80-100"	100-120"	120"+
Panhysterectomies	2	12	49	27	55
Supervaginal hysterectomies	2	17	37	16	58
Other Laparotomies	7	18	54	31	44
Total	11	47	140	74	157

NOTE:—Hysterectomies almost invariably included perineorrhaphy and incidental appendectomy. Other pelvic laparotomies included routine curettage, cauterization of the cervix, or plastic, incidental appendectomy, together with operations for ectopic pregnancy, salpingitis, ovarian pathology, and retroversion of the uterus.

The three types of operations were almost equally divided in this series.

In 30 minor operations in which avertin was used plus gas-oxygen-ether anesthetic, 16 patients, or 53 per cent, had neither nausea nor vomiting after the operation. Nine, or 30 per cent, vomited.

In 69 minor operations in which avertin was used (always in moderate doses) *without* ether, 43 patients, or 62 per cent, had neither nausea nor vomiting, and only 12, or 17 per cent, actually vomited.

#### SODIUM AMYTAL

We were interested to see the effect of sodium amytal combined with small doses of avertin, and we have used it in 22 gynecologic operations, which were just reviewed. Only 5 of these patients vomited, i.e., 17, or 77 per cent, did not. However, it is important to know if the patient has any idiosyncrasy to sodium amytal, consequently 3 gr. are given the night before the operation, and, if there are no untoward results, 6 gr. are given in the morning one-half hour before the avertin.

This insures the patient's being completely asleep when she leaves her room, a fact which has frequently been commented upon with



enthusiasm by the patient. No morphine is given in these cases before operation, and only with extreme caution immediately afterwards.

We have used this combination very beneficially in the cases of 30 cesarean sections, in which the use of morphine preoperatively was not thought advisable. In such cases a weight 15 or 20 pounds less than the real weight was used in computing the dosage, to compensate for the weight of the baby, amniotic fluid, and placenta.

On one occasion morphine gr.  $\frac{1}{6}$  and atropine gr.  $\frac{1}{150}$  were inadvertently given after the sodium amytal and avertin, and this patient was so deeply anesthetized that a complete perineal repair and hemorrhoidectomy were performed before the patient needed any inhalation anesthetic for the laparotomy.

#### MORTALITY

Four patients, in 564 cases, died while in the hospital:

1. With tuberculous meningitis, three days postoperative
2. General peritonitis, fourteen days postoperative
3. Cardiac death, two days postoperative

4. An obese negress who died in 1931 had a 90 mg. dose of avertin per kilogram, was in a state of shock on the operating table, and never recovered from it. Diagnosis: Intraligamentous fibroid. Operation: Supravaginal hysterectomy; she died three hours postoperative, without regaining consciousness. Autopsy was refused. This may have been death from the anesthetic.

#### SEVERE IMMEDIATE COMPLICATIONS

In 1930 there were 18; in 1931, only 3; in 1932 and 1933, only 2; and in 1934, only 1.

The severe immediate complications, that of rapid and dangerous drop of blood pressure, with other evidences of shock, are in direct proportion to the dosage of avertin used. Needless to say, some patients were not in as good condition for any operative procedure as they might have been; but when the dosage is considered, the symptoms are readily explained. In 1930 a dose of 90 to 100 or more milligrams of avertin was not uncommon, and symptoms of shock were of frequent occurrence, either during the operation, or immediately after.

The picture is that of profound shock with marked drop in blood pressure: the respirations become very shallow or cease; the pulse, weak and thready; color, pale or slightly cyanotic; and the skin, clammy. It has been proved experimentally that there is not only splanchnic dilatation but also engorgement and dilatation of the coronary arteries. As a cardiac depressor, however, it is said to be only one-sixteenth as toxic as chloroform (Parsons').

Treatment includes shock position, application of heat, caffeine and ephedrin hypodermically, intravenous saline or glucose, inhalation of

carbon dioxide, 4 to 10 per cent, alpha lobeline to stimulate the respiratory center, and artificial respiration.

Now to return to observations of this particular group of cases, it was noted that headache occasionally occurs the day of the operation but quickly disappears.

Pulmonary complications have been conspicuously absent, but this bears out the observation of others in this respect. The one woman who died had atelectasis, though hers was a cardiac death, proved at autopsy; there were no cases of postoperative pneumonia in the entire series. This may be ascribed to the fact that the amount of ether required is a great deal less than in those not receiving this premedication.

For a time it was thought that pentobarbital sodium would give the same desirable preanesthetic assistance, and indeed it does in some instances, without any fear of inducing shock. However, barbiturates often bring on severe excitability, which is not desirable during the several hours immediately following any operation.

#### NAUSEA AND VOMITING

Nausea and vomiting during the first twenty-four hours after any gynecologic operation is not desirable. With ether anesthesia it is the rule, rather than the exception, so that one frequently sees postoperative orders which say, "Give water when nausea ceases," or words to that effect. It is a safe assumption that not more than 10 per cent of all patients given an ether anesthetic escape severe nausea or vomiting.

This percentage is increased if nitrous-oxide-oxygen anesthesia is used with only small amounts of ether, but we have never seen any inhalation anesthetic that could be given with less nausea than following avertin premedication.

#### SUMMARY

We have made a critical study of 429 major gynecologic operations, noting the time consumed. Most of these cases included at least a perineorrhaphy in addition to the operation noted.

The time of actual operation was over two hours in 157, or 36 per cent, of these.

The absence of nausea or vomiting within twenty-four hours of operation as an evidence of good anesthesia has been reviewed in 465 cases, which showed that 198 patients were nauseated; the remainder, or 59.5 per cent, had neither. Only 117 actually vomited, leaving 348, or 75 per cent, who did not.

Among the 99 minor procedures, 59, or 58 per cent, had neither nausea nor vomiting, and 78, or 79 per cent, had no vomiting.

Giving sodium amytal with avertin has a marked hypnotic effect, and the patient is more certain to be asleep when she leaves her room, but it does not appear to influence the postoperative comfort.

The dose of avertin has gradually been diminished so that now only 60 or 70 mg. per kilogram of body weight is used. This is especially important in the obese patient or in one with hypertension.

Avertin should not be used if deep relaxation is required because it is impossible to obtain this on account of diminution of the respiratory volume. Serious complications have practically disappeared since the dose of avertin has been reduced.

#### CONCLUSIONS

1. Avertin is safe as a basal anesthetic in gynecology if the known contraindications and dangers are heeded.

2. It should be given by a trained anesthetist, experienced in the administration of rectal anesthesia.

3. The dose that is safe is usually not more than 70 mg. per kilogram of body weight. Serious complications attend administration of large doses, though postoperative nausea is greatly reduced.

4. Avertin can be combined with a barbiturate if it is known that there is no idiosyncrasy on the part of the patient. This insures a light sleep before leaving the patient's room, which is of marked advantage in the care of many excitable women.

5. Within twenty-four hours postoperative nausea has been found to be absent in 59 per cent of these patients, and no vomiting occurred in 75 per cent.

6. Postoperative nausea and vomiting have been found to be in direct proportion to the concentration of ether used in the inhalation anesthetic.

NOTE.—I wish to thank Mrs. Gertrude Fife and Miss Mary Lucile Goodman, of the School of Anesthesia at Lakeside Hospital, for their aid and cooperation in procuring the data which have been presented.

#### REFERENCES

- (1) *Eichholtz, Fritz*: Deutsche med. Wchnschr. 53: 710, 1927. (2) *White, Charles S.*: Ann. Surg. 94: 888, 1931. (3) *Bourne and Raginsky*: Am. J. Surg. 14: 653, 1931. (4) *Shipley and Karns*: Tr. Sect. Surgery, General & Abd., A. M. A. p. 54, 1930. (5) *Field and Pilcher*: Ann. Surg. 57: 577, 1933. (6) *Barlow, O. W., Fife, G. L., and Hodgins, A. C.*: Arch. Surg. 29: 810, 1934. (7) *Parsons, F. B.*: Canad. M. A. J. 24: 59, 1931.

10515 CARNEGIE AVE.

---

Ohga, T., and Aoji, Sh.: *Trichomonas Vaginalis Among Japanese Women*, Jap. J. Obst. & Gynec. 17: 364, 1934.

The authors examined 1,000 women for trichomonas vaginalis and found these organisms in 124. The incidence during pregnancy was almost the same as among nonpregnant women. Relatively few women suffer any discomfort, and only 36 out of the 124 women had any subjective symptoms. The authors failed to find any increase in puerperal morbidity among women who had trichomonas vaginalis during pregnancy.

J. P. GREENHILL.

AN EXPERIMENTAL STUDY OF THE EFFECTS OF INTRA-  
VENOUS INJECTIONS OF HYPERTONIC GLUCOSE  
SOLUTION (50 PER CENT) ON THE CIRCULATION OF THE CAT

II. EFFECTS OF INJECTION OF 50 PER CENT GLUCOSE SOLUTION BEFORE  
AND AFTER ARTIFICIAL REDUCTION OF BLOOD PRESSURE BY TRAUMA\*

VINCENT P. MAZZOLA, M.D., AND MARCUS A. TORREY, B.S.,  
BROOKLYN, N. Y.

*(From the Departments of Obstetrics and Gynecology and Physiology, Long  
Island College of Medicine)*

EXPERIMENTALLY,<sup>1</sup> we have found that 50 per cent glucose injected into the circulation of the cat will raise blood pressure and pulse pressure and will diminish pulse rate, and that preliminary injection of glucose makes experimental reduction of blood pressure by hemorrhage more difficult. Cannon and Bayliss,<sup>2</sup> in their studies on traumatic shock, demonstrated that trauma to one of the extremities of the experimental animal produces general phenomena that are closely similar to those seen in patients in shock. It has advantages over other methods of producing a fall in blood pressure in that the opposite extremity can be used as a control, and in the fact that the inflow and outflow of blood from the part can be controlled as desired. It is, therefore, the purpose of this paper to report the effects of injection of 50 per cent glucose into the circulation of cats, both before and after the experimental reduction of blood pressure by trauma.

METHODS

Cats were used in all experiments. Sodium amytal (0.1 to 0.2 gm.) injected intraperitoneally was employed as the anesthetic. The animals were anesthetized sufficiently with this amount to permit no evidence of pain when the posterior extremity was traumatized. Mean blood pressure readings were determined by placing a cannula in the carotid artery which was connected to a mercury manometer. A needle was placed in the femoral vein and connected with a buret carrying the solutions. At times the buret was replaced by an ordinary Luer syringe when rapid injections were desired.

The amount of glucose used was 6 c.c. of a 50 per cent solution (2 c.c. per kilogram of body weight). Both the slow and rapid methods of injection were used. The rapid injections were made with a Luer syringe, delivering a maximum of 8.5 c.c. per minute. In the slow method, the buret was used and the cock was set so that it delivered approximately 1 c.c. per minute.

\*Read by invitation at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, November 22, 1932, and later revised to include work done in 1932 but published in 1933.

Experimental trauma was obtained by applying a tourniquet to the posterior leg, high up in the groin, and crushing the tissues below with a heavy pair of mechanics pliers. Care was taken that the bone was not broken and the skin not torn. The length of time of traumatization was ten minutes; this was always done by the same person. The tourniquet was released within five to ten minutes following the trauma and the experiment continued. This method of producing shock is almost identical with the method described by Cannon and Bayliss.<sup>2</sup>

### EXPERIMENTAL RESULTS

The effects of the intravenous injection of 6 c.c. 50 per cent glucose into the circulation of cats, with an artificial reduction of blood pressure by injury to the leg, were determined in twenty experiments. Two groups are presented: one in which no glucose was given before trauma, and the other in which 6 c.c. of 50 per cent glucose were injected before trauma. Both groups received glucose following the leg injury.

#### CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA (INJURY TO LEFT LEG)

##### *Group I. Without Previous Glucose (10 cats).*

1. *Blood Pressure:* Following trauma the blood pressure fell an average of 20.7 mm. Hg. When glucose was administered (6 c.c. of 50 per cent), the pressure began to rise, reaching a high level average of 98 mm. Hg, or 7.33 mm. above the original. Hence, following glucose the pressure rose so that the fall was obliterated, and the sustained level was slightly above normal (average normal 82.66. Hg average sustained level after glucose injection, 84.66 mm. Hg, see Tables I, II, and III).

TABLE I. TEN CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA FOLLOWED BY INJECTION OF GLUCOSE

	ORIGINAL	TRAUMA	6 C.C. 50% GLUCOSE
Blood pressure (mm. Hg)	82.66	61.33	84.66
Pulse pressure (mm. Hg)	3.66	3.75	5.41
Pulse rate (per min.)	143.0	138.3	128.0

TABLE II. TEN CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA WITH GLUCOSE BEFORE AND AFTER TRAUMA

	ORIGINAL	6 C.C. 50% GLUCOSE	TRAUMA	6 C.C. 50% GLUCOSE
Blood pressure (mm. Hg)	87.3	104.30	91.3	106.60
Pulse pressure (mm. Hg)	3.66	5.66	4.33	6.33
Pulse rate (per min.)	155.0	146.60	134.0	126.60

TABLE III. TWENTY CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA

	NO GLUCOSE BEFORE TRAUMA—INJURY LEFT LEG	6 C.C. 50% GLUCOSE BEFORE
Blood pressure (mm. Hg)	-21.33	-13.0
Pulse pressure (mm. Hg)	+ 0.09	No change
Pulse rate (per min.)	- 4.70	-12.6

2. *Pulse Pressure:* The final pulse pressure was increased above the original. Trauma showed an increase of 0.66 mm. Hg. After glucose, the pulse pressure showed a further increase of 1 mm. Hg (see Tables I, II, and III).

3. *Pulse Rate:* There was a definite decrease in the pulse rate. A final average difference of 15 beats per minute (see Tables I, II, and III).

*Group II. With Previous Glucose (10 cats).*

1. *Blood Pressure:* The original injection of 6 c.c. 50 per cent glucose elevated the blood pressure above the original, from 87.3 mm. to 104.3 mm. Hg. Following

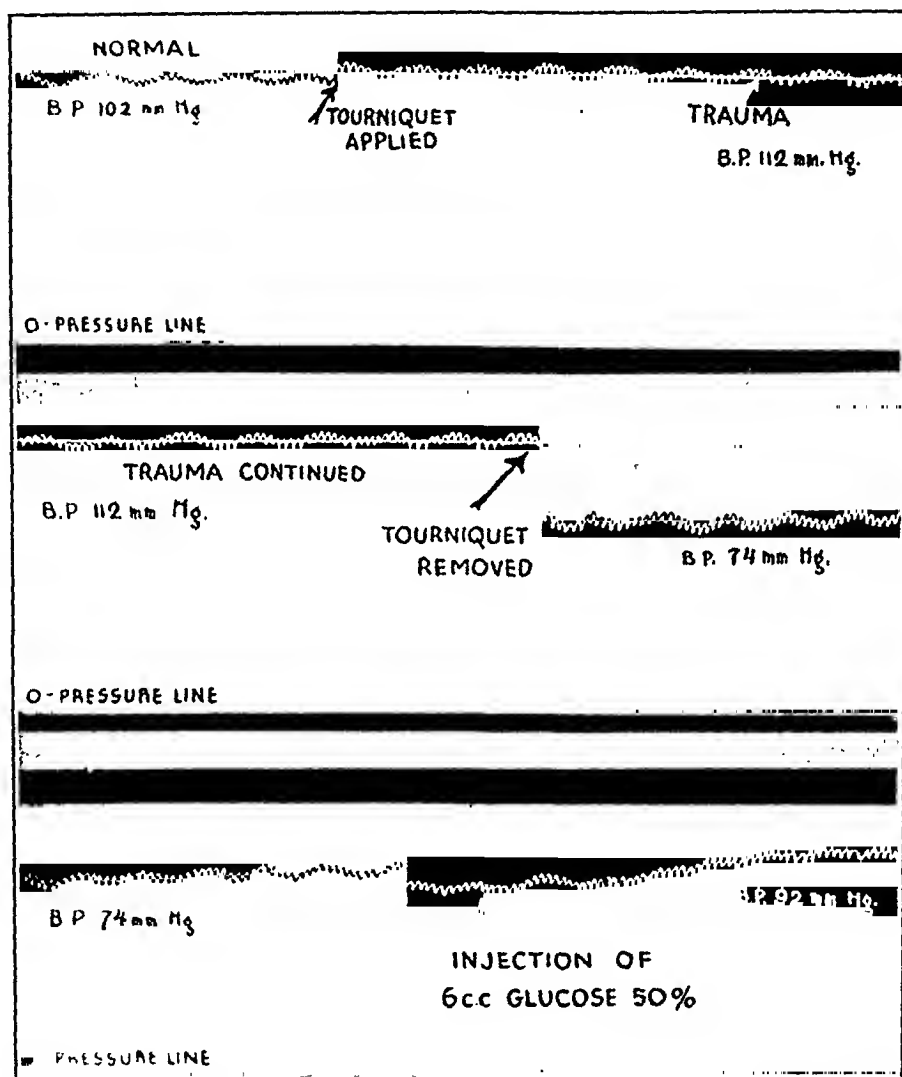


Chart 1.—Response to injection of 6 c.c. of 50 per cent glucose after trauma—injury to left leg.

trauma the blood pressure fell sharply, but the low level was only a few millimeters below the previous normal (80.6 mm. Hg). Within less than one minute the blood pressure began to rise so that the sustained pressure increased, reaching a high point of 108.0 mm. Hg. This was maintained at 106.6 mm. Hg (i.e., 19.3 mm. above the original (see Tables II and III).

2. *Pulse Pressure:* The pulse pressure was increased as a rule. In one case it returned to normal (see Tables II and III).

3. *Pulse Rate:* The pulse rate in all cases was slowed an average of 29 beats per minute (see Tables II and III).

#### DISCUSSION

Injection of 50 per cent glucose into cats, with a blood pressure artificially reduced by trauma, produced a characteristic reaction in all cases. There was always a rise in blood pressure, an increase or a return to the original pulse pressure, and a slowing or a return to the

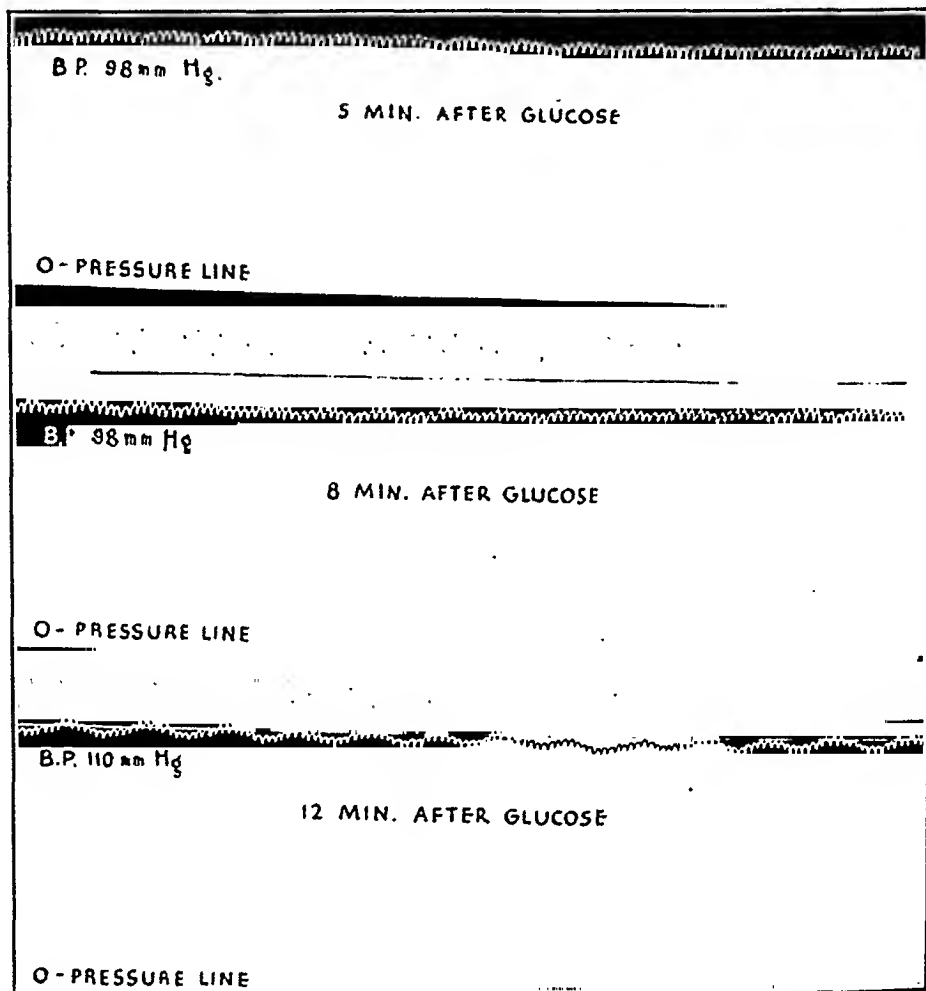


Chart 2.—Continued response to injection of 6 c.c. 50 per cent glucose after trauma—  
injury to left leg.

original pulse rate. The initial degree of fall in blood pressure upon the release of the tourniquet following trauma was about the same whether glucose had been given previously or not. But in cats in which a fortifying dose had been given, there was the tendency for the blood pressure to rise again subsequent to the trauma. The sustained fall in blood pressure in this series was less than the fall in the animals without the previous injection of glucose. Hence, the final maintained blood pressure level was much higher after trauma when glucose had been previously

given. These findings would indicate that a fortifying dose of glucose resists the fall in blood pressure following artificial reduction of blood pressure by trauma.

Following the administration of glucose after trauma the blood pressure was increased as a rule. The pulse pressure was closer to the

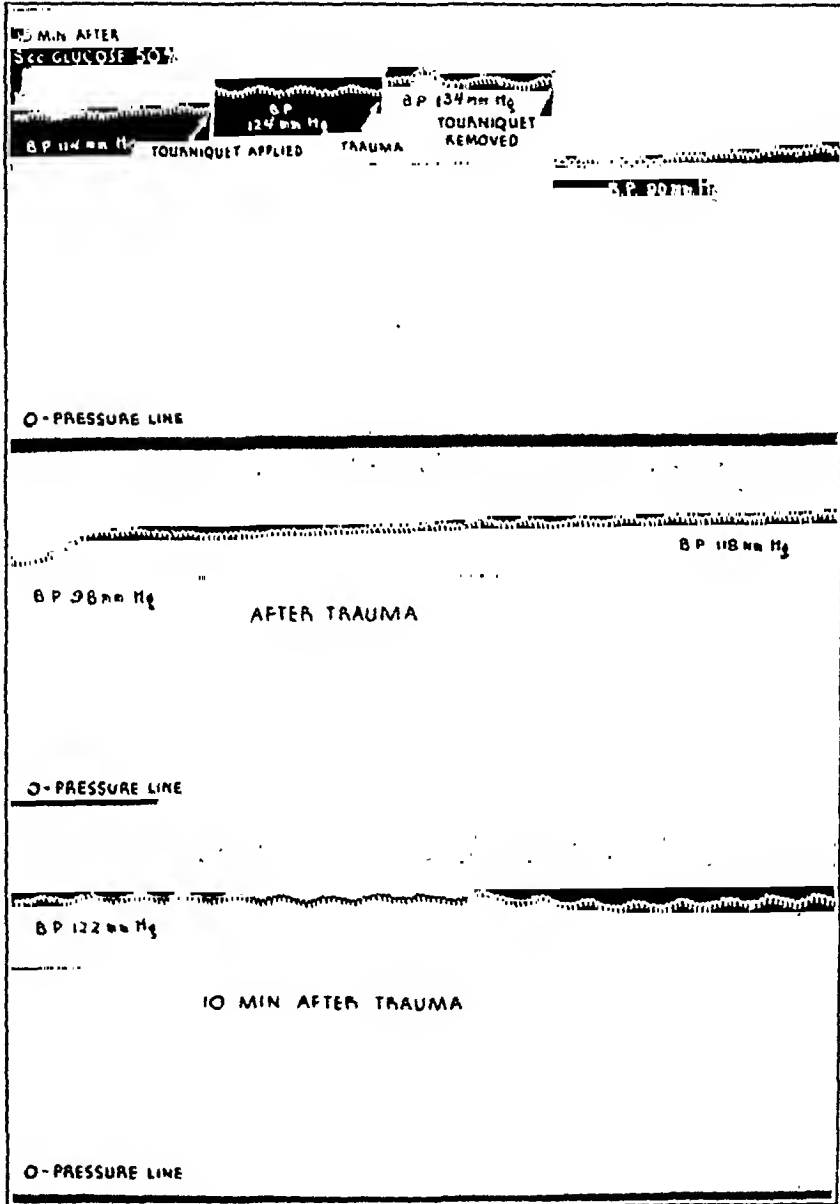


Chart 3.—Response to trauma fifteen minutes after injection of 6 c.c. of 50 per cent glucose.

original in the series of animals that had received previous glucose than in those cases in which no initial glucose was given. The pulse rate in all cases was slowed after glucose injection.

Tables I, II, and III present the significant average findings. Charts 1, 2, 3, and 4 are characteristic tracings taken from both groups.



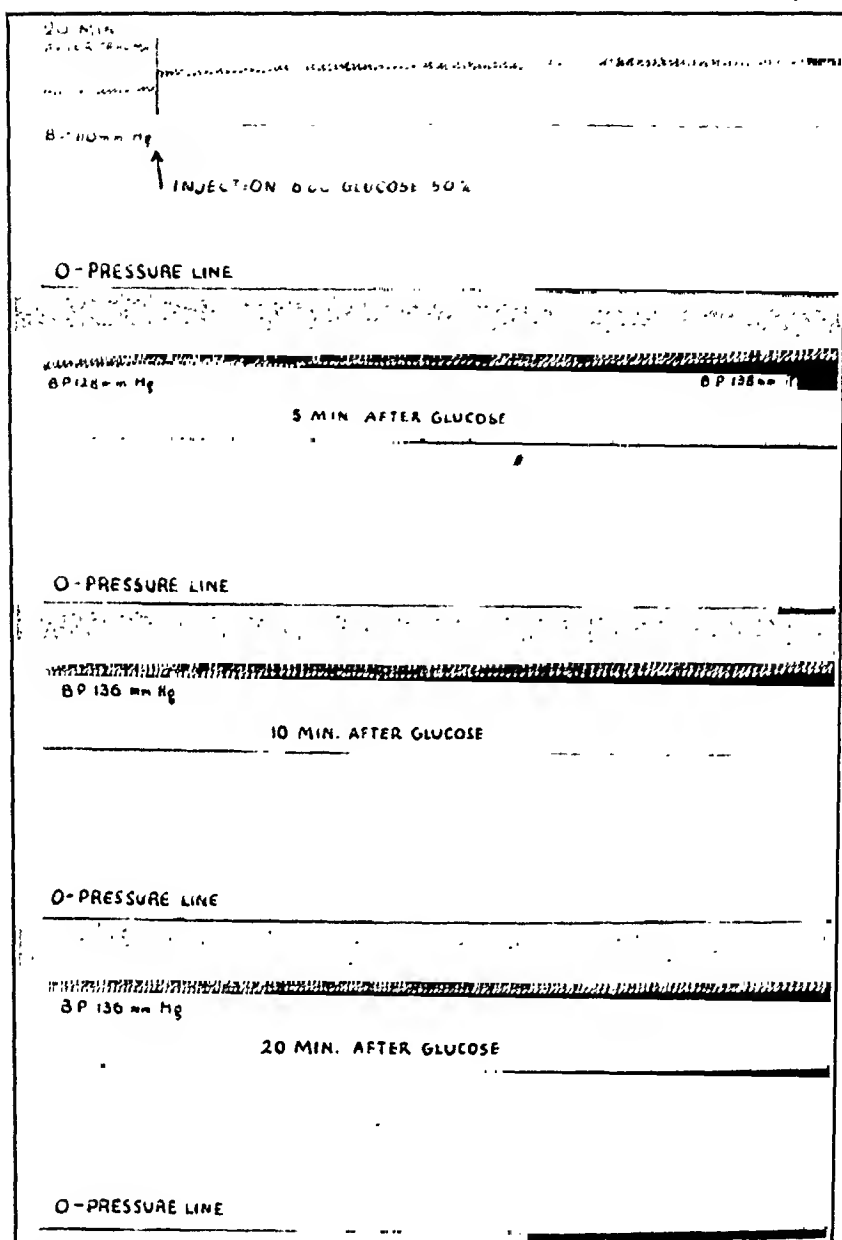


Chart 4.—Response to second injection of 6 c.c. of 50 per cent glucose twenty minutes after trauma with previous administration of glucose.

#### SUMMARY AND CONCLUSIONS

In experiments on cats anesthetized by intraperitoneal sodium amytal, the effects of the intravenous injection of 50 per cent glucose before and following trauma to one of the extremities were studied. As a result of our findings we conclude that:

1. Fifty per cent glucose injected intravenously into cats with a blood pressure artificially reduced by trauma produces a sustained rise in blood pressure.
2. It causes a sustained rise in pulse pressure.

3. It produces a sustained diminution in pulse rate.
4. Preoperative injection of 50 per cent glucose diminishes the fall in blood pressure due to trauma.

## REFERENCES

- (1) *Mazzola, V. P., and Torrey, M. A.*: AM. J. OBST. & GYNEC. 25: 643, 1933.
- (2) *Cannon and Bayliss*: Note on Muscle Injury in Relation to Shock Report of Shock Committee, Medical Research Committee, No. 26, pp. 19-23, March, 1919.

133 CLINTON STREET

## BLASTOMYCOSIS OF THE FEMALE REPRODUCTIVE TRACT\*

## WITH REPORT OF A CASE

E. C. HAMBLÉN, M.D., R. D. BAKER, M.D., AND D. S. MARTIN, M.D.,  
DURHAM, N. C.

(From the Departments of Obstetrics and Gynecology, Pathology, and Bacteriology,  
Duke University School of Medicine)

GENERALIZED blastomycosis (American Blastomycosis, Gilchrist's disease) can no longer be considered a clinical rarity in view of the numerous case reports in the recent literature. The fungus has been known to produce lesions in almost every organ in the body, including the male reproductive organs. Infection of the body of the uterus and of the tubes has never been described to our knowledge. This may be because blastomycosis is comparatively rare in women and not because the reproductive organs of the female have increased resistance to infection with this fungus. Less than a tenth of the reported cases of systemic blastomycosis occurred in this sex.

There is a report of primary blastomycosis of the cervix in a Paraguayan woman.<sup>1</sup> A biopsy of the cervix showed miliary abscesses and double contoured bodies but no giant cells or blastomycotic tubercles. The organisms could not be cultivated. Palpation indicated that the deeper pelvic organs were not involved.

No account of significant blastomycotic lesions of the vagina was found. References to fungous infections of the vagina were usually concerned with monilia,<sup>2</sup> and it was not definite that the yeasts found in cases of vaginitis had an etiologic bearing. Castellani stated<sup>3</sup> that fungi are frequently encountered in vaginal discharges but that he never noted the fungus described by Gilchrist.

The following case is added to the literature as the first recorded case of blastomycotic infection of the endometrium, myometrium and

\*Submitted for publication June 4, 1935.

tube. It is of further interest in that the diagnosis was established by examination of the curettings before laparotomy.

*Clinical Report.*—Mrs. V. S., aged twenty-seven years, white, para 3-0-3, was first seen by the gynecologist on Apr. 2, 1935, when she was referred by the orthopedist because of irregular, too frequent and profuse menses (polyhypermenorrhea). She had been under observation and treatment by the medical and orthopedic services since July, 1934, because of blastomycosis of the lungs and a compression fracture of the twelfth dorsal vertebra. Menstrual irregularities were first noted upon the return of menses following the birth of her last child, Nov. 27, 1933, when menses began to occur approximately every three weeks with increase in the duration of the flow from four to seven days and a proportional increase in the amount of blood loss as judged by napkin count and pad saturation. During the past several months prior to admission, the menses had been very irregular and excessive. The last menstrual period began fifteen days prior to admission and still persisted at the time patient was first seen. The period previous to this had occurred seven days before and lasted only one day. Two weeks before this, there had been an excessive period of 'seven days' duration. There had been no unusual symptoms associated with these irregular menses except evident weakness due to excessive blood loss. The patient complained also of abdominal symptoms which had become more pronounced in the last six to eight months. Low grade lower abdominal pain and tenderness increased. The patient had noticed some "swelling of the abdomen" and "bulging" when she was upright. Constipation had become more severe during this time. There had been no obstructive symptoms; appetite had been good.

Family history was unimportant. Past health had been good until the past year. An attack of "kidney colic" occurred in March, 1934; three cystoscopic treatments were received. A hemorrhoidectomy was performed in April, 1934. Her back was injured by a fall in April, 1934. Pain in the chest and a productive cough of three months' duration caused the patient to be seen in Duke Hospital for the first time, July 8, 1934. A diagnosis of pulmonary blastomycosis was made from pus obtained by bronchoscopic examination. Treatment with iodides, vaccines, and x-ray resulted in satisfactory arrest of the pulmonary condition. A fracture of the twelfth dorsal vertebra resulting in progressive weakness of the lower extremities was discovered at this admission. This was treated with splints and braces by the orthopedists. A definite diagnosis of blastomycosis of the spine was not made. The patient was discharged from the hospital Oct. 23, 1934. There had been four subsequent admissions to Duke Hospital (Dec. 3-6, 1934; Jan. 22-24, 1935; Feb. 4-6, 1935; Apr. 1-25, 1935, present admission) for observation and treatment of her pulmonary and spinal condition during which time progressive improvement had been reported.

Marital history included three normal pregnancies, labors, and puerperia, all children being alive and well; the youngest child was born Nov. 27, 1933. The patient lived in a small hamlet in North Carolina; cared for own household; had not been overworked; and was of temperate habits.

*Physical Examination.*—The patient was well nourished and well developed, and was in no acute distress. Her weight was 136 pounds. General physical examination was essentially negative except for evidences of the fractured vertebra and the pelvic findings. No abnormal signs were elicited on chest examination, and the x-ray examination showed the old lesion in the upper left lobe well healed. The orthopedic condition showed improvement; there was slight weakness of the lower extremities; however, the patient was able to walk with the use of the braces with which she had been supplied. Pelvic examination showed a moderate relaxation of the perineal floor with moderately atonic levator muscles, with a slight rectocele and slight sagging of the bladder base. The external genitals were normal otherwise.

Bartholin's and Skene's glands and urethra were normal. The cervix was of normal consistency, directed slightly upward, movable with moderate pain. Speculum examination showed a slight chronic endocervicitis of the ulcerative type. There was moderate old serosanguineous vaginal discharge. The uterus was in midposition, slightly softened, of approximately normal size, moderately fixed, and movable with moderate pain. There were two masses about 3 to 3½ inches in diameter, quite tender and relatively firm, one upon each of the lateral surfaces of the uterus. The mass on the right side was more lateral and was situated in about the midportion of the pelvis. The mass on the left side, which was slightly larger than the one on the right side, was associated with the posterior and lower surface of the uterus and seemed to be rather firmly fixed to the culdesac. Neither of these masses could be separated completely from the uterus. Tubes and ovaries could not be outlined as such. No other pelvic masses could be felt. A preliminary diagnosis was menorrhagia and metrorrhagia (probably of inflammatory origin, chronic endometritis) and bilateral tuboovarian masses. A blastomycotic infection of the pelvic organs was considered in view of the patient's previous record. The possibility of peritonitis from the same organisms was suspected because of the abdominal symptoms. A diagnostic curettage was advised in order to establish the etiology of the bleeding.



Fig. 1.—Fragment of curettings from uterine cavity showing endometrial blastomycosis. An organism with double contour lies in the center of the figure. Upward and to the right is a giant cell. The stroma shows subacute and chronic endometritis. Upward and to the left is endometrial epithelium.  $\times 200$ .

*Laboratory Findings.*—Hemoglobin 72 per cent (Sahli); R.B.C., 3,720,000; W.B.C., 16,050; differential: polymorphonuclear leucocytes 83 per cent, large mononuclear leucocytes 2 per cent, small mononuclear leucocytes 12 per cent, transitionals 0 per cent, eosinophiles 2 per cent, basophiles 1 per cent; blood cells of normal morphology. Urinalysis: (noncatheterized) yellow, clear, 1,009, acid, no sugar, no albumin, no acetone, 5-7 white blood cells, no red blood cells, no casts. Sedimentation time 6 mm. in first 30 minutes.

*Operative Findings and Treatment.*—On Apr. 4, 1935, examination under  $N_2O$  and  $O_2$  anesthesia revealed no additional abnormalities. Dilatation and curettage yielded a moderate amount of endometrium from which diagnosis of blastomycosis of the endometrium and endocervix was made by one of us (see pathologic report). Blastomycetes were cultured from swabs taken from the uterine cavity at the time of curettage (see bacteriologic report).

Possible methods of treatment were discussed after determining the infecting agent. It was decided to perform a laparotomy with removal of the uterus and tuboovarian masses. In arriving at this decision we consulted with members of our own department and with Dr. D. T. Smith. We felt that little benefit could be expected

from curettement alone in the presence of the bilateral tuboovarian masses. We believed that radiation of the pelvic viscera in the presence of such evident infection was not justified and that the results of such radiation of the active ovarian tissue would be more harmful than surgical ablation. It was felt that, if the infection were localized to the pelvis and if all of the involved tissue could be removed, the ultimate prognosis might be good; however, if there were extensive abdominal and peritoneal involvement, as the history suggested, the removal of the pelvic focus would be beneficial although the prognosis would still be grave. The possibility of poor healing of the abdominal wound with fistulas had to be considered. Dr. Smith thought the patient could tolerate surgical anesthesia and that no anxiety should be felt because of possible trouble from her previous pulmonary lesions.

Laparotomy was performed on Apr. 8, 1935, following routine preoperative preparation. Anesthesia was induced with nitrous oxide and oxygen and then was changed to drop ether. The abdomen was opened through the usual midline incision. Approximately four quarts of clear straw-colored fluid were aspirated from the peritoneal cavity. Inspection showed a diffuse involvement of the pelvic parietal peritoneum with multiple small grayish miliary tubercle-like nodules about 1 mm. in diameter. The omentum which had come well down into the pelvis and was adherent to the matted pelvic viscera was studded with similar nodules. The sigmoid was adherent to the left side of the pelvic mass and several loops of small intestine were bound by dense adhesions to the upper portion of the mass. These, as well as other loops of intestine in the lower abdomen, showed studding similar to that appearing on the peritoneum. The anterior surface of the uterus was firmly adherent to the vesical peritoneum. In several areas of the broad ligaments the nodules coalesced and appeared as grayish plaques. The intestinal and omental adhesions were freed carefully by sharp dissection, ligated, and cut so that finally the pelvic masses could be outlined. The uterus, which was adherent in its anterior and upper surface to the bladder and the bladder peritoneum, was of normal size and in anterior position. The right tube was red, thick, tortuous, about 1 inch in thickness, and arched acutely down into the culdesac, where it was densely adherent to a right tuboovarian mass about 3 inches in diameter. This mass was densely adherent to the undersurface of the right broad ligament which was about  $\frac{3}{4}$  inch thick, and to the lower right border of the uterus and to a loop of small intestine (Fig. 2). The mass was freed carefully by blunt and blind dissection and in the process of delivery ruptured, expelling about 10 c.c. of creamy, thick yellow pus which were aspirated and reserved for bacteriologic examination. The tuboovarian mass was freed from its broad ligament and uterine attachments and removed. The left tube, thickened and tortuous, was not as enlarged or as indurated as the right one. It measured approximately  $\frac{1}{2}$  inch in its greatest diameter. It was also intimately associated with a tuboovarian mass about  $3\frac{1}{2}$  inches in diameter which lay beneath the left broad ligament and was adherent to the culdesac. The mass was partially covered anteriorly by the sigmoid to which it was adherent. The mass was freed by blunt dissection and, in the process of delivery, ruptured. About 15 c.c. of thick creamy pus were aspirated and were saved for examination. The tuboovarian mass was excised. Supravaginal hysterectomy and routine pelvic repair were done. A Penrose drain was inserted well down into the culdesac and brought out through the left low abdominal stab wound. The appendix was left untouched. The abdomen was closed in the usual manner, and the usual dressings applied.

The patient stood the operative procedure and anesthesia well. Her pulse was 92 at the conclusion of the operation.

Postoperative care, in addition to the usual measures, included placing patient in moderate Fowler's position as soon as she reacted sufficiently, withholding fluids and nourishment by mouth for five days, and supplying saline by hypodermoclysis.

Postoperative convalescence was good except for a rapid pulse rate, as high as 140, which gradually became normal by the fifth postoperative day. Highest postoperative temperature was 38.6° C., reached on the second day. Temperature was normal on the sixth day. There was no rise in the leucocyte count. Distention was not marked. Skin clips and drain were removed on the fifth day. Wound showed healing by first intention, and site of drainage filled in rapidly. Wound was dressed

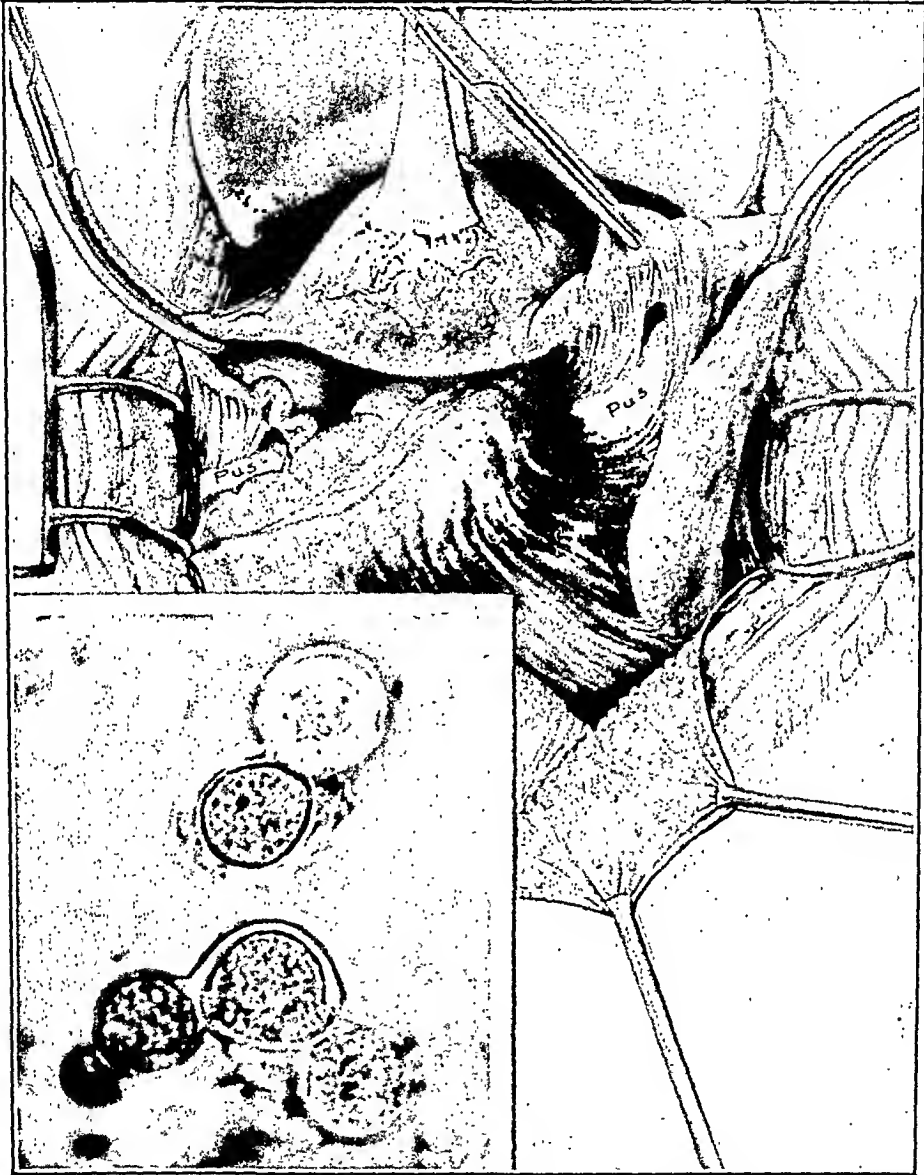


Fig. 2.—Appearance of pelvis and lower abdomen at laparotomy. The enlarged right tube, the bilateral pelvic abscesses, and the studding of the peritoneum with the blastomycotic tubercles are shown. Insert shows a fresh smear preparation of pus from the pelvic abscesses stained with tincture of iodine.

frequently and painted with 1 per cent aqueous solution of gentian violet. On the eleventh day all the silkworm-gut sutures were removed; a small stitch abscess was found about one silkworm-gut suture; culture of this showed no blastomycetes but hemolytic *staphylococcus aureus*. The patient complained of a catching pain in the left lower chest on the fifteenth day. Dr. Smith could find no abnormal chest signs, and an x-ray picture of the chest showed no recent change. The patient was dis-

charged from the hospital Apr. 25, 1935. The abdominal wound was well healed, and the pelvic condition was satisfactory except for moderate induration in both adnexal regions. She was to continue the use of braces, to continue potassium iodide, and she was referred to her local physician for further dressings and observation. In reports from patient, May 25, 1935, no untoward symptoms were described.

*Comments on Clinical Course.*—One is led to suspect from the duration of menstrual symptoms that the pelvic involvement occurred early in the course of the disease. This is in accord with the pathologic findings (q. v.).

The choice of surgery proved to be wise as shown by the postoperative course. Poor healing and fistulas had been anticipated. Gentian violet (aqueous solution) was used in liberal quantities, especially for irrigation of the drainage site because of its inhibiting action on the growth of blastomycetes, as shown by Sanderson and Smith.<sup>4</sup>

It is possible that the earlier treatment of this patient with a combination of vaccines and potassium iodide played an important rôle in making her a good sub-

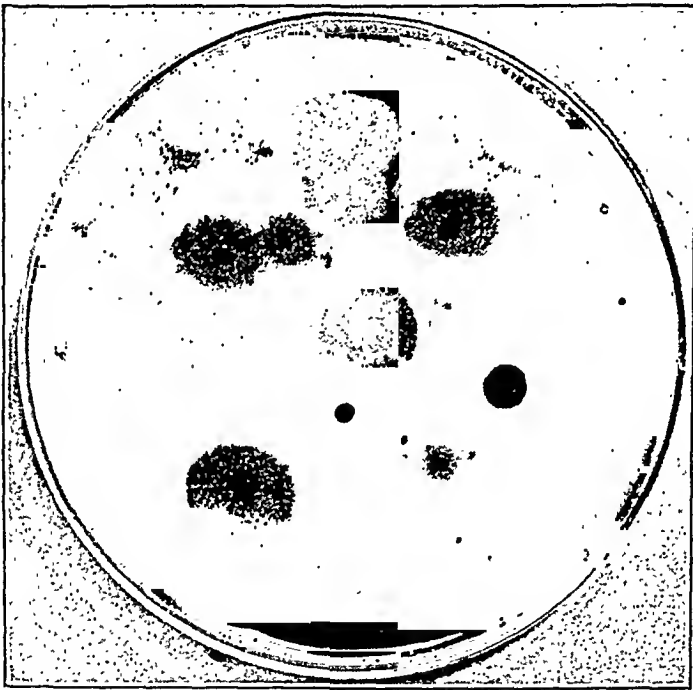


Fig. 3.—Blood agar plate inoculated by mincing a small portion of the uterus with seissors and streaking heavily over the plate. Two colonies of *Staphylococcus albus* were planted on the plate for comparison. The plate was photographed after eight days' growth at room temperature.

ject for operation. In spite of the fact that she had had the disease for more than a year, her general state of health seemed excellent.

The prognosis is, of course, guarded, but it is felt that a large residual focus was removed and that with continuation of the medical treatment, the ultimate result may be good.

The details of medical treatment will be the subject of a future communication by Smith and Martin.<sup>5</sup>

#### BACTERIOLOGIC STUDY

As noted in the case history, blastomycetes were seen in smear and cultured from the pus obtained at bronchoscopy.

At the time of curettage, swabs were planted on blood agar slants and dextrose agar slants. Eight colonies of blastomycetes appeared after eight days' incubation at room temperature.

At operation cultures were made of the peritoneal fluid, left tube, left ovary and uterus. Fresh smears all showed numerous budding, double-contoured blastomycetes (see Fig. 2 for appearance of organisms in pus from the peritoneal cavity). The solid bits of tissue were minced with sterile scissors and smeared over the surfaces of blood agar and dextrose agar plates and incubated at room temperature and at 37° C. All cultures yielded blastomycetes, but it was interesting to note that the fungus grew more rapidly on blood agar plates incubated at the lower temperature (Fig. 3).

Morphologically and culturally the fungus isolated from this patient conforms in all details to the organisms isolated from many other cases of generalized blastomycosis. The cultural characteristics have been adequately described by Stober,<sup>6</sup> Benham,<sup>7</sup> and many others. Serologic studies by one of us<sup>8</sup> have shown that the fungus obtained from this patient was identical with the blastomycetes of four other cases of generalized blastomycosis.

Complement fixation tests with different strains of blastomycetes were made at frequent intervals throughout the course of the disease, and all tests were strongly positive with all strains of blastomycetes tested. The complete protocols of the complement fixation tests with serum from this patient are reported elsewhere.<sup>8</sup>

#### PATHOLOGIC STUDY

The tissue from the curettage of the uterine cavity formed a mass which amounted to less than 1 c.c. in volume. The individual pieces measured 1 to 3 mm. across, and were soft and pinkish gray.

The microscopie section of the curettings, which had been embedded in paraffin, sectioned, and stained with hematoxylin and eosin, showed endometrial tissue for the most part, but fragments of endocervix were also present.

The cellular exudate in the pieces of endometrium consisted of polymorphonuclear neutrophils in large numbers, eosinophils in small numbers, and varying numbers of lymphocytes, plasma cells, and large mononuclear cells. Giant cells were noted rarely. One giant cell contained well over a hundred nuclei. In addition to the cellular reaction, there was much fibrosis, but no tubercles.

Double-contoured bodies (Fig. 1), free and also within giant cells, were seen in the endometrial stroma. Approximately a dozen bodies occurred in the whole section. The average diameter was from two to four times that of a red blood cell. The peripheral ring was hyaline and the central part either clear or provided with several granules which stained with the hematoxylin. One of the bodies, enclosed within a giant cell, had knoblike processes or buds.

The same tissue reaction was noted in some of the fragments of endocervix.

The blastomycetes were similar in all respects to the organisms observed in a case of generalized blastomycosis which had come to necropsy.

The diagnosis of blastomycosis of endometrium and endocervix was made.

The tissue received from the abdominal operation four days after the curettage of the uterine cavity consisted of the body of the uterus, the right tube, the left tube and ovary, and a piece of omentum.

The body of the uterus was little if any enlarged. It measured 5 cm. from the level of amputation to the top, 3.5 cm. anteroposteriorly, and 5.5 cm. from side to side. The serosal surface showed several red fibrous thickenings. Sagittal section of the uterus (Fig. 4) disclosed a narrow uterine cavity with a brown discoloration which extended 2 mm. into the uterine wall. Multiple parallel slices on each side of the midline showed nothing additional.

The right tube was in two pieces (Fig. 5). The longer, cone-shaped part, measuring 10.5 cm. in length and 2.5 cm. in greatest diameter, was attached to the



uterus by the narrow end and the distal end was yellow, granular, and fibrous. The other piece of right tube, which was at first thought to be the right ovary, measured 4.5 by 3 by 2.5 cm. One end corresponded to the distal end of the longer piece of tube. The serosa of both pieces was red, rough and covered with granular and taglike excrescences. Longitudinal section of both pieces showed a thickened, scarred peripheral zone and a central yellow, opaque, firm region. In the very center

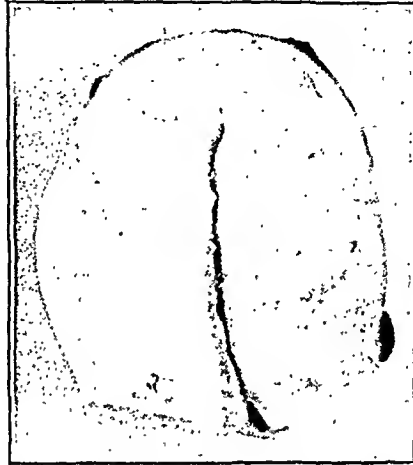


Fig. 4.—Sagittal section of uterus. Curettage had been performed and accounts for some of the discoloration lining the cavity. The deeper part is due to blastomycosis. Most of the myometrium appears normal. The fibrous peritoneal thickenings are evident as darker surface elevations.



Fig. 5.—The right tube, eroded into two pieces. The narrow tapering end of the longer piece was attached to the uterus.

the tissue was friable and pus was noted, especially in the narrow end of the longer piece. The shorter piece contained a cavity 1 cm. in diameter. Sections of both pieces were made at various levels, but nothing resembling ovarian tissue was noted.

Apparently the right tube had been eroded through at a point about two-thirds of the distance from the uterus to the fimbriated end.

The fallopian tube on the left was 3.5 cm. long. The surface was rough, but the tube contained none of the yellow tissue seen in the right one.

The left ovary measured 3 by 2 by 2 cm. The surface was red and granular, but its substance was free of the blastomycotic process.

The piece of omentum had a scarred exterior.

Microscopic sections of the uterus showed that the red fibrous serosal thickenings noted grossly consisted of vascular scar tissue in which tubercles occasionally occurred. The same peritoneal reaction was noted on the surfaces of both tubes, the left ovary, and the piece of omentum.

At the fundus of the uterus, where the endometrium had not been removed by the curette, there were tubercles with central giant cells, both in the endometrial stroma and in the immediately subjacent myometrium (Fig. 6). Blastomycetes were fairly frequent in the giant cells.

Along the cavity, just above the level of amputation, the tubercles extended as much as 4 mm. into the uterine wall. They were of two types, those with central giant cells and those with centers of pus. Further out in the myometrium there was moderate perivascular lymphocytic and plasma cell infiltration, but no tubercles.



Fig. 6.



Fig. 7.

Fig. 6.—Section from the fundus of the uterus showing two blastomycotic tubercles in the endometrium (upper right) and three in the myometrium (lower left).  $\times 33$ .

Fig. 7.—Section of the two pieces of right tube. There is extensive fibrosis of the walls, and pus occupies the narrow, uterine end of the longer piece.  $\times 12$ .

There was no widespread active process extending in an uninterrupted fashion from the uterine cavity into the tubes since microscopic sections of the interstitial portions of each tube showed only some granulation tissue beneath the epithelium.

A large microscopic section of the two pieces of the right tube (Fig. 7) demonstrated the great fibrous thickening of the peripheral part of the tube with many polymorphonuclear neutrophiles infiltrating this fibrous layer. More centrally, tubercles were numerous, and eosinophiles were present. Blastomycetes were visible under low magnification. Most of the tubercles had central giant cells as in the endometrium (Fig. 6). Others had a central area of pus and an encircling zone of fibrous tissue (Fig. 8). In several places great collections of giant cells containing blastomycetes were noted (Fig. 9). The eroded surfaces of the pieces of the tube presented small areas of necrosis, and necrotic tissue was also seen on the outside of the tube in a few places.

The longitudinal folds of the tubal mucosa were partly preserved and were swollen and infiltrated with lymphocytes and other cells. In addition, the central region

showed an interesting irregular proliferation of mucosal epithelium, undoubtedly due to attempts at regeneration. Within the tube there was almost no necrosis or caseation. The lumen was, on the other hand, filled with blastomycotic granulation tissue. The more proximal, narrow part of the tube was filled with pus (Fig. 7) consisting of polymorphonuclear neutrophils and a few macrophages and giant cells. The organisms in the pus were both free and within giant cells.

The distal part of the tube and some of the fibrous tissue adherent to the outside of the proximal portion were studied further in several microscopic sections, but no tissue resembling an ovary was located.

A section of the left tube revealed only a minimal degree of inflammatory reaction about the lumen, consisting of a few lymphocytes beneath the intact epithelium.

The section of the left ovary showed no involvement of the ovary itself, although the surface was covered with blastomycotic granulation tissue.

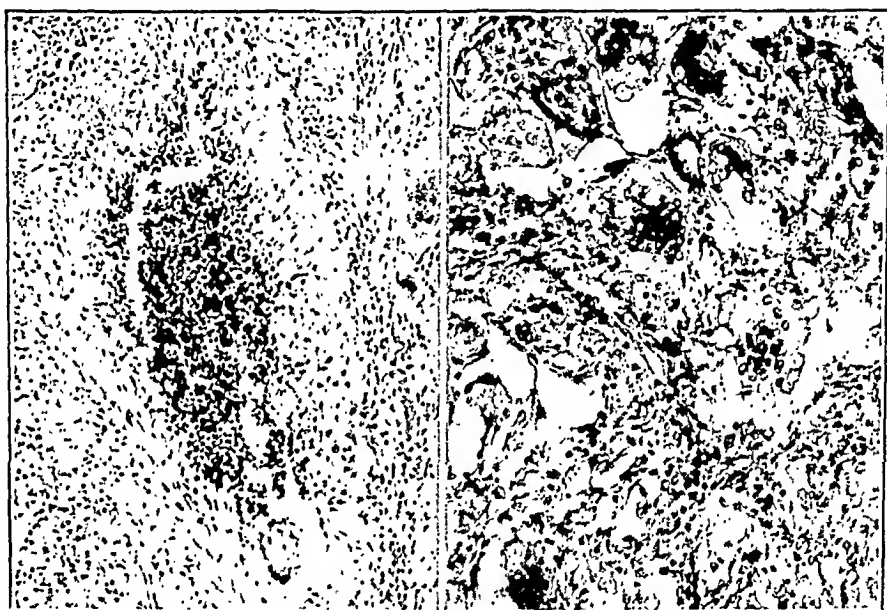


Fig. 8.

Fig. 9.

Fig. 8.—Miliary abscess in wall of tube, with surrounding fibrosis and adjacent giant cells.  $\times 135$ .

Fig. 9.—Giant cell reaction in wall of tube. Many of the paler bodies within the giant cells are blastomycetes.  $\times 215$ .

A search was made for tubercle bacilli in sections of the uterine cavity and of a part of the right tube which contained pus, giant cells, and caseation. No acid-fast organisms were noted, while a control section from a known case of tuberculosis stained simultaneously showed numerous acid-fast organisms. In addition, the counterstain of Loeffler's methylene blue failed to show any other kind of bacteria in the present case.

A diagnosis of blastomycosis of the right fallopian tube, endometrium, myometrium, and peritoneum was made.

Summarizing the pathologic findings, the lesions which have just been described could be divided into at least four forms.

First, the most prominent appearance was that of nodules or tubercles with giant cells which often contained the blastomycetes. These tubercles were especially numerous in the wall of the tube, but were also to be seen along the uterine cavity (Fig. 6) and in the peritoneum. Second in prominence were abscesses. They were chiefly

miliary abscesses with dense fibrous walls (Fig. 8). These, like the tubercles, occurred in both uterine wall and tube. Organisms could usually be found in or about them. Larger accumulations of pus, such as that free in the proximal end of the tube and those in the abscess pockets on the posterior side of the broad ligament, belonged to the same group. A much less conspicuous place was taken by a third form of tissue change, that of necrosis. This occurred at the eroded junction point of the two pieces of tube and also on the outside of the tube, probably in relation to the abscess pockets. It looked much like the caseation of tuberculous, but it was undoubtedly due to the blastomycetes, since other organisms could not be demonstrated in or about it. The fourth type of change was that of fibrosis, which was extensively developed in the tube and on the peritoneum.

The specific forms of reaction just enumerated represented the progressive development, over a long period of time, of the exudative and proliferative response of the tissue. The conglomeration of these processes in the region of the nodules and miliary abscesses gave the appearance of blastomycotic granulation tissue, a term which might be applied as appropriately to blastomycotic lesions as the term tuberculous granulation tissue is applied to tuberculous lesions.

In brief, the tissue reactions in the operative material corresponded to what has been repeatedly described in reported cases of blastomycosis.

Gilchrist and Stokes<sup>9</sup> wrote that the lesions were characterized by "the production of miliary abscesses and the formation of tubercle-like nodules."

Hektoen<sup>10</sup> wrote as follows concerning the morphologic changes in blastomycosis:

"Study of human material as well as material from inoculated animals shows that the microorganisms in question may induce the formation of an inflammatory granulation tissue with numerous giant cells of the Langhans type associated with more or less extensive suppuration. The relative predominance of proliferative or suppurative processes appears to vary under various conditions. In loose connective tissues, such as the subcutaneous, there seems to be a distinct tendency to abscess. Microscopically, the more or less nodular lesions in which the proliferative changes are well marked present certain general resemblances to those of tuberculosis."

That the general appearance of the lesions, both grossly and microscopically, is remarkably like that of tuberculosis has been emphasized repeatedly. D'Aunoy and Beven<sup>11</sup> in reporting a series of cases of blastomycosis, stated that "only the presence of the specific organisms either active or dead, allowed making an histologic differentiation from tuberculosis in any of the cases."

This statement applies with equal force to our case.

It is interesting to speculate regarding the entrance and spread of the blastomycotic process in the body of the patient.

How did the organisms originally enter the patient's body?

The patient had apparently never had cutaneous blastomycosis from which the generalized lesions might have developed. D'Aunoy and Beven state that "usually, the occurrence of visceral blastomycotic involvement is secondary to cutaneous lesions caused by the parasites; but . . . systemic involvements need not necessarily be secondary to cutaneous manifestations, or at least can occur as sequelae to superficial lesions not sufficiently grave to cause notice thereof to be taken."

Stober put more emphasis on the respiratory tract as the portal of entry of the organisms: "In at least fourteen of the cases reported the first symptoms were referable to the lungs, and of eleven necropsies in these cases, nine presented old bronchopneumonic lesions. It is also possible that the subcutaneous abscesses or cutaneous lesions marking the onset in other patients were due to unrecognized pulmonary lesions with metastases in the skin and elsewhere."

How did the uterus and right tube become infected?

The tissue reaction in the right fallopian tube appeared older than that in the uterus since the former showed far more fibrosis. The spread seemed therefore to have been from the fallopian tube to the uterine cavity and to the peritoneum. There was probably a hematogenous dissemination from the lungs with a colonization of the organisms in the tube, from which they spread to the uterine cavity and to the peritoneum. This type of spread is analagous to what probably occurs in tuberculosis, the tissue reaction of which is much like blastomycosis. Had the organism, like the gonococcus, entered by the vagina, an infection of the cervical canal, with early symptoms from that region and an advanced process there or in the uterine cavity at the time of operation, might have been expected.

#### SUMMARY

Recorded cases of fungous infection by blastomycetes of the female reproductive tract were not found in the literature, with the exception of one instance of cervical blastomycosis.

A case is reported of infection of the fallopian tube and uterus with *Blastomyces dermatitidis* in a patient with arrested pulmonary blastomycosis (American type, Gilchrist's disease). A preoperative diagnosis of uterine involvement was made from a section of endometrial curettings and confirmed by culturing the organism.

Myelologic and anatomic studies of the removed tissues are recorded. These constitute apparently the first report of extensive blastomycosis of the female reproductive tract. The tissue reaction in the affected organs was remarkably like that in tuberculosis but was to be differentiated from the latter by the presence of the double-contoured blastomycetes.

The removal of the uterus was necessary to prevent further excessive blood loss, and the extirpation of the tuboovarian masses was apparently indicated to eliminate the large blastomycotic focus. The uncomplicated postoperative course seemed to have justified surgery in this case.

#### REFERENCES

- (1) Ocana, T.: Rev. méd. del Rosario 21: 797, 1931. (2) Plass, E. D., Hestline, H. C., and Borts, I. H.: AM. J. OBST. & GYN. 21: 320, 1931. (3) Castellani, A.: J. Trop. Med. 34: 396, 1931. (4) Sanderson, E. S., and Smith, D. C.: Arch. Dermat. & Syph. 16: 153, 1927. (5) Smith, D. T., and Martin, D. S.: (To be published). (6) Stober, A. M.: Arch. Int. Med. 13: 509, 1914. (7) Benham, R. W.: Arch. Dermat. & Syph. 30: 385, 1934. (8) Martin, D. S.: J. Infect. Dis. (In press). (9) Gilchrist, T. C., and Stokes, W. R.: Bull. Johns Hopkins Hosp. 7: 129, 1896. (10) Hektoen, L.: J. A. M. A. 49: 1071, 1907. (11) D'Aunoy, R., and Beven, J. L.: J. Lab. & Clin. Med. 16: 124, 1930.

## AN ANALYSIS OF LABOR IN YOUNG GIRLS

A. CHARLES POSNER, M.D., F.A.C.S., AND MICHAEL PULVER, B.S., M.D.,  
NEW YORK, N. Y.

*(From the Obstetric Service of Harlem Hospital)*

AT HARLEM HOSPITAL, in New York City, 17,048 obstetric patients were admitted during the period from 1923 to 1933, inclusive. Of that large number, 100 were girls between the ages of twelve and fifteen. It was believed that a presentation of the course of labor and of infant and maternal morbidity and mortality would prove of interest.

The percentage of the cases in this young group to all obstetric cases in the ten-year period at Harlem Hospital is 0.58 per cent, or a ratio of 1 to 170.

Of the 100 young mothers, 2 were twelve years old, 10 thirteen years old, 26 fourteen years old, and 62 fifteen years old.

Ninety-nine of the 100 patients were primiparas. For 1932, 41 per cent (745 cases) of all obstetric cases in Harlem Hospital were primiparas, while 59 per cent were multiparas.

Ninety-three of the patients in our study were delivered in the hospital, while the remaining seven patients were delivered by outside physicians or midwives and brought to the hospital for postpartum care. These will be designated as Groups I and II, respectively. The term premature birth applies to newborn infants weighing between 1,500 and 2,500 gm.; miscarriage, to those weighing less than 1,500 gm.; and full term, to those weighing over 2,500 gm.

TABLE I. BIRTH STATISTICS AND MORTALITY

	GROUP I	GROUP II
Total number of babies	94	7
Full term { Livebirths	77	3
{ Stillbirths	2	1
{ Neonatal deaths	0	0
Premature { Livebirths	10	2
{ Stillbirths	0	0
{ Neonatal deaths	0	1
Miscarriages	5	1
Twin pregnancies	1	0

The total number of livebirths was 92 out of 101 for both groups, or 91.8 per cent. For the group which was delivered in the hospital, the ratio is 87 livebirths out of 94, or 92.6 per cent.

The average weight of 79 full-term babies was 6 pounds, 9½ ounces. The mean weight was 6 pounds, 8 ounces.

The ratio of the sexes of the babies born to the twelve- to fifteen-year group was 53 males to 41 females for the hospital deliveries. The ratio for all deliveries on the obstetric service in 1932 was 51 males to 49 females.

TABLE II. ANALYSIS OF UNCORRECTED FETAL AND NEONATAL MORTALITY

	12-15 YEAR GROUP 1923-33 101 BIRTHS		OBSTETRIC SERVICE, 1932					
			ENTIRE SERVICE 1658 BIRTHS		CLINIC 1210 BIRTHS		NONCLINIC 448 BIRTHS	
	NO.	%	NO.	%	NO.	%	NO.	%
Stillbirths								
Full term	3	2.98	18	1.85	15	1.23	3	0.67
Premature	0	0	48	2.89	22	1.81	26	5.80
Miscarriages	6	5.95	63	3.79	22	1.81	41	9.15
Total fetal mortality (full term and premature)	3	2.98	66	4.74	37	3.04	29	6.47
Total stillbirths	9	8.91	132	8.71	62	5.09	70	15.62
Neonatal mortality								
Full term	0	0	26	1.56	18	1.48	8	1.78
Premature	7	6.93	34	2.05	20	1.65	14	3.12
Previa	0	0	23	1.39	6	0.49	17	1.40
Total neonatal mortality (full term and premature)	7	6.93	60	3.60	38	3.13	22	4.90
Fetal and neonatal mortality (full term and premature)	10	9.90	126	8.35	75	6.17	51	11.37
Total infant mortality	16	15.84	215	12.96	106	8.71	109	22.92

In analyzing the figures of fetal and neonatal mortality in Table II, we note that, while stillbirths at term were 60 per cent greater in the twelve- to fifteen-year group than in the entire obstetric service for 1932, premature stillbirths did not occur in the young group, while in the entire service there were 48 of 1,658 cases, or 2.89 per cent. These were mainly nonclinic emergency cases, 26 of 448 total cases, or 5.8 per cent. Miscarriages were 32 per cent more numerous in the young group than in the general service, the ratio being 5.95 per cent to 3.79 per cent. It will be seen that, of the nonclinic emergency cases, 9.15 per cent were delivered of miscarriages, while there were only 1.81 per cent miscarriages among the regular clinic cases. Total stillbirths were practically the same in both groups, 8.91 per cent for the young group and 8.71 per cent for the service. The regular clinic group, however, yielded 5.09 per cent stillbirths of the 1,210 births, while the nonclinic emergency group showed a stillbirth mortality of 15.62 per cent of 448 births.

The neonatal mortality for the young group was 6.93 per cent, all premature. This was three and a half times as high as the percentage of premature neonatal deaths for the entire obstetric service. The

figure was four and a half times that recorded for the regular clinic group, but only two and a half times higher than in the nonclinic emergency group.

Total infant mortality, including fetal mortality, miscarriages, and neonatal deaths, was 15.84 per cent for the young group, as contrasted with a mortality of 12.96 per cent for the entire service. For clinic cases, the percentage of infant mortality in the whole service was 8.71 per cent, and for nonclinic emergency cases, 22.92 per cent.

The Wassermann or Kahn test was made a routine part of the obstetric service in 1928. Of the 93 hospital deliveries in the young group, there is a report for 58 cases. With 1-, 2-, 3-, or 4-plus reactions regarded as positive, the percentage for the young group was 8.62 per cent, while the whole service yielded 309 positive reactions from 1,784 cases tested, or 17.32 per cent.

TABLE III. PRESENTATIONS

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total babies (including one twin pregnancy)	94	Total babies	1658
Vertex	92.55%	Vertex	93.10%
L.O.A.	57		
L.O.T.	1		
L.O.P.	1		
R.O.A.	24		
R.O.T.	2		
R.O.P.	2		
Breech	5.32%	Breech	6.09%
R.S.A.	3		
R.S.P.	1		
L.S.A.	1		
L.S.P.	0		
Undetermined	2		

TABLE IV. STATE OF PELVIS

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total cases	93	Total cases	1658
Ample	82.75%	Ample	87.5%
Deformed	17.25%	Deformed	12.5%

Antepartum complications for the twelve- to fifteen-year group totaled 16, or 17.22 per cent, while the total for the entire obstetric service for 1932 was 314 of 1,805 admissions, or 17.39 per cent.

The percentage of intrapartum complications in the twelve- to fifteen-year group was 13.98 per cent, or 12 of 93 cases. For the whole obstetric service in 1932, the incidence of intrapartum complications was 19.32 per cent, or 321 of 1,658 cases.



The operative incidence in the twelve- to fifteen-year group was practically the same as in the entire service for 1932. In the young group there were 87.2 per cent spontaneous and 12.8 per cent operative deliveries; for the service the figures are 87.5 per cent spontaneous and 12.5 per cent operative deliveries. These figures exclude episiotomies performed in both groups.

TABLE V. CONDITION OF PERINEUM

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total cases	93	Total cases	1658
Intact	67.74%	Intact	80.75%
First deg. lacer.	24.73%	First deg. lacer.	14.90%
Second deg. lacer.	6.45%	Second deg. lacer.	4.34%
Third deg. lacer.	0.0	Third deg. lacer.	0.06%
Episiotomies	9.74%	Episiotomies	6.80%

The incidence of postpartum complications in the young group was 23, or 24.7 per cent; and in the whole service, 23.5 per cent.

The incidence of morbidity in the young group was high. The guide used was the presence of a temperature of 100.4° F. for two days, exclusive of the first day. The ratio of morbidity was 21 cases in 93, or 22.6 per cent. The incidence of morbidity for the entire service in 1932 was 10.2 per cent of 1,658 cases.

For the young group, the fetal complications totaled 5, or 5.3 per cent of 94 infants. They included one case of spina bifida, one case of hallux valgus, and three cases of fetal distress.

In Table VI we have compared mortality rates for the twelve- to fifteen-year group with those for the entire service during 1932, divided into clinic and nonclinic cases. The maternal mortality per 10,000 livebirths has also been indicated. The figures in Table VI are

TABLE VI. MATERNAL MORTALITY

	CASES	DEATHS						PER 10,000 LIVE BIRTHS	NUMBER OF LIVE BIRTHS
		TOTAL		PUERPERAL		NON- PUERPERAL			
		NO.	%	NO.	%	NO.	%		
12-15 year group, 1923-33									
Delivered in hos- pital	93	3	3.2	3	3.2	0	0.0	345	87
Not delivered in hospital	7	0	0.0	0	0.0	0	0.0	0	5
Totals	100	3	3.0	3	3.0	0	0.0	326	92
Entire obstetric service, 1932									
Clinic cases	1331	12	0.9	9	0.67	3	0.22	104	1141
Nonclinic cases	474	8	1.6	6	1.26	2	0.42	206	378
Totals	1805	20	1.1	15	0.83	5	0.27	131	1519

in agreement with the findings of the Department of Labor for thirteen states in 1927, and for those states and two others in 1928. Their maternal mortality statistics are as follows: for colored females, 109 per 10,000 livebirths; for all females under fifteen, 161 per 10,000 livebirths; for colored females under fifteen, 235 for 10,000 livebirths.<sup>1</sup>

As mentioned previously, there were seven patients who were delivered by others outside the hospital and brought there for postpartum care. These patients were all fifteen years of age. The puerperium was uneventful in two, parametritis occurred in one, morbidity in three, and cardiac complications in one. There were no maternal deaths in this group. The infant mortality is given in Table I.

The following are the case histories of the three patients who died postpartum. All were hospital deliveries.

M. S., a fifteen-year-old primiparous white female, was admitted to the obstetric service as a nonclinic emergency case on April 4, 1926. Labor had begun five hours and forty minutes before admission. When the patient was admitted, the fetal head was on the perineum. Ten minutes after admission, she was delivered of a normal child from an L.O.A. position; the child weighed 7 pounds, 14 ounces. The patient sustained a first-degree laceration of the perineum. Condition following delivery was good.

On admission, temperature was 100° F., and pulse 76. Urine was negative. Temperature was flat until the second day, when it suddenly rose to 101° F.; it reached 103° F. on the third day, and 104.4° F. on the fifth day, following which it dropped to normal and remained so until the seventh day. On that day the urine showed hyaline casts, a few leucocytes, and acetone, but no diacetic acid.

On the eighth day the temperature rose to 105.2° F. Blood culture on the same day revealed seven colonies of hemolytic streptococci per cubic centimeter, and on the ninth day 70 colonies of hemolytic streptococci per cubic centimeter within ten hours. The blood count on the tenth day showed 6,200 white cells, of which 70 per cent were polymorphonuclear leucocytes, and 30 per cent lymphocytes. On the eleventh day postpartum, blood culture showed 98 colonies of hemolytic streptococci per cubic centimeter within twenty-four hours.

The patient's temperature continued very high, and, despite three blood transfusions and continued stimulation, it rose to 107.8° F. on the thirteenth day postpartum, when the patient died.

Diagnosis: Septicemia (*Streptococcus hemolyticus*) and terminal bronchopneumonia.

B. S., a fifteen-year-old primiparous colored female, was admitted to the Obstetric Service of Harlem Hospital at 8:30 A.M. on March 7, 1925, as a nonclinic emergency case. The patient had been in labor for twelve hours prior to admission. Half an hour after admission, the patient was delivered spontaneously of a male child weighing 5 pounds, 8 ounces. She sustained a first-degree laceration of the perineum.

On admission, temperature and pulse were normal. On the third day postpartum, temperature suddenly rose to 103° F., and pulse to 140. Temperature continued between 103° F. and 105° F. until the twelfth day, when it dropped to 101.6° F., pulse 120.

On the fifth day postpartum, the patient began complaining of cough. The next day there was exquisite tenderness in both lower quadrants and foul lochia. Vaginal examination revealed induration of both fornices, tenderness, and heat in the vagina. Parametritis was diagnosed on the tenth day. On the twelfth day a diagnosis of

bronchopneumonia was made by the pneumonia service. After lapsing into unconsciousness, the patient died at 5:10 A.M. on March 19, twelve days postpartum.

Diagnosis: Bilateral parametritis and terminal bronchopneumonia.

M. B., a fifteen-year-old, single, primiparous, colored girl, was admitted to the Obstetric Service of Harlem Hospital on Jan. 8, 1931, at 8:35 P.M., with a history of having been in labor for forty-nine hours and thirty-five minutes. Pains were occurring every five minutes. The membranes had ruptured an hour before admission.

The patient had received adequate prenatal care. She had registered at the prenatal clinic on Sept. 4, 1930, and had made six antepartum visits in all. Her family, personal, and medical histories were all negative. The Wassermann reaction was likewise negative. The abnormal findings were breech presentation, umbilical hernia, and a generally contracted pelvis.

On admission, blood pressure was 110/54, temperature 99° F., pulse 88, respiration 22, fetal heart 150. The presenting parts were unengaged. Rectal examination revealed two and one-half fingers' dilatation of the cervix; no vaginal examination was made.

Approximately four hours after admission, the patient was delivered spontaneously of a living female child, weighing 6 pounds, 1 ounce. The second stage of labor lasted thirty-four minutes. There was a first-degree laceration of the perineum, which was sutured with one suture of No. 1 chromic catgut. The third stage of labor was prolonged, and the placenta was expressed one hour and twenty-four minutes after delivery. Hemorrhage was slight. The patient was given 1 c.c. of pituitrin at the end of the third stage.

On the third day postpartum, January 12, the patient began to complain of abdominal pain and vomiting. She vomited a huge amount of green fluid. The uterus was one finger below the umbilicus and very tender. The abdomen was markedly distended, with tenderness and rigidity over both lower quadrants. A diagnosis of parametritis and pelvic peritonitis was made. Temperature was 103° F., pulse 120, respiration 28, and blood culture negative. Abdominal puncture, made to rule out the possibility of pneumococcic peritonitis, showed streptococcus formation. Lung findings were negative. The patient was very toxemic.

Vaginal examination on the ninth day revealed a dry mucous membrane and a relaxed perineum; the external os and the internal os each admitted the tip of a finger. The uterus was four fingers above the symphysis pubis. The abdomen was distended, and there were marked tenderness and rigidity over the umbilicus. Urine was negative. Blood count taken on the ninth day showed white blood corpuscles 19,400, polymorphonuclear leucocytes 82 per cent, lymphocytes 17 per cent, and transitionals 1 per cent.

On the tenth day postpartum the pulse ranged between 110 and 160. Temperature fluctuated between 100.2° F., and 105° F. Despite blood transfusions, clysis, and stimulation, the patient died on the eleventh day postpartum.

Diagnosis: Puerperal sepsis.

#### SUMMARY AND CONCLUSIONS

1. The ratio of births in the age group twelve to fifteen years in the years 1923-1933 to all births at Harlem Hospital, proved slightly higher than the ratio shown in the statistics of the Census Bureau for 1927. The incidence of primiparity for the young group was two and a half times that of the entire service at the Hospital, which, considering the age limits, is entirely logical.

2. The percentage of stillbirths at term was 60 per cent higher in the young group than in the whole service for 1932, and miscarriages were 32 per cent more numerous in the young group. However, premature stillbirths were nonexistent in the young group, and therefore the percentage of total stillbirths was practically the same in both groups. The percentage of neonatal deaths in the twelve- to fifteen-year group was three and one-half times as high as the figures for the whole service.

3. In the young group, birth weights of infants were half a pound less, on the average, than in the service proper for primiparas.

4. Positive Wassermann or Kahn reactions were half as frequent in the young group as in the general service. Evidently syphilis is acquired by the female later in life.

5. The ratio of vertex to breech presentations was practically the same in both groups. The percentage of ample pelvises in the young group was lower, however, the ratio being 82.75 per cent to 87.50 per cent. The percentage of lacerated perineums was also definitely higher, due to the 99 per cent primiparas in the young group.

6. While antepartum complications were practically the same in both groups, intrapartum complications were 40 per cent lower in the twelve- to fifteen-year group. The operative incidence was the same for both groups. Postpartum complications were a trifle higher in the young group.

7. Morbidity was more than twice as high in the young group as in the entire service. This is a disquieting factor and shows less fitness for pregnancy in the young group (as might be expected from the age limits twelve to fifteen) than is possessed by the older group in the service.

8. In comparing maternal mortality in the young group with maternal mortality in the entire service for 1932, it should be remembered that the ratio of patients was 100 to 1,805. On the basis of these figures, the mortality of the young group was three times that of the general service. In addition, all deaths in the young group were in the acute emergency cases.

9. It should be noted that all three deaths in the young group followed spontaneous deliveries, and that there were no postoperative deaths.

10. The importance of prenatal care should also be noted, for two of the three patients who died postpartum received no antepartum care.

#### REFERENCE

(1) U. S. Department of Labor: *Maternal Mortality in Fifteen States*, U. S. Children's Bureau Publication No. 223, Washington, Government Printing Office, 1933.

1132 PARK AVENUE

1437 LELAND AVENUE

## TREATMENT OF THE PERSISTENT OCCIPITOPOSTERIOR POSITION BY 180 DEGREE MANUAL ROTATION OF THE OCCIPUT

SAMUEL S. ROSENFELD, M.D., F.A.C.S., NEW YORK, N. Y.

IT IS only too well known to those who practice obstetrics that the persistent occiput posterior and to a lesser degree the persistent occiput transverse are very frequent causes of maternal exhaustion, fetal embarrassment and delayed delivery.

The incidence of posterior position is given as less than 1 per cent by Tweedy<sup>1</sup> in 13,511 deliveries, while Williams<sup>2</sup> reports 11.3 per cent in 5,000 cases. In 2,365 cases Piper<sup>3</sup> found an incidence of 17.1 per cent, which also included occiput transverse positions. At the Philadelphia Lying-In Hospital, Piper noted an incidence of 29 per cent.

If all patients were examined by experienced attending obstetricians at the onset of labor instead of by internes, the figures quoted in the preceding paragraph would undoubtedly be found far too low. Percentages for the incidence of the posterior and transverse positions at the commencement of labor will have to be enormously increased since the thorough anatomic researches by Caldwell, Moloy and D'Esopo.<sup>4</sup> They have proved by x-ray that the great majority of labors begin as occiput posterior or occiput transverse.

It is probable that in the vast majority of cases, the occiput, at the commencement of labor, is either transverse or posterior. In most of these patients anterior rotation takes place and delivery is spontaneous. Interference is necessary only in those cases where anterior rotation fails to take place and where the occiput persists in remaining either posterior or transverse.

In a small percentage of cases the occiput is delivered posteriorly. In these cases birth is either spontaneous or is effected by forceps. There are several methods of coping with or correcting these positions. Most of them are efficient and not very hard to master.

Since these cases are very likely to be long and drawn out, practically all authorities are agreed that watchful waiting and some sort of analgesia is the proper treatment for the first stage of these labors. During this stage some advise that the patient lie on that side toward which the fetal back is directed, thereby favoring anterior rotation. Some claim good results with tight abdominal binders.

After the cervix is fully dilated or fully dilatable various means are employed to hasten or effect delivery, by internal podalic version, the

Scanzoni or the modified Scanzoni maneuver. The Kjelland and, to a lesser degree, the Barton forceps are used by some, especially in persistent transverse positions. Manual rotation of the head has been found successful by a few and some textbooks recommend it.

The Pomeroy maneuver was introduced by the late Ralph Pomeroy of Brooklyn. Unfortunately, he never published the procedure. The only reference in the literature to the Pomeroy maneuver is a paper entitled "The Pomeroy Maneuver in the Treatment of the Persistent Occipitoposterior Position," by Aranow.<sup>5</sup>

The Pomeroy maneuver consists in rotating the posterior fetal shoulder. The rest of the fetus follows this rotation. In order to prevent the head from rotating back again to its original position, he advised and practiced overcorrection, i.e., from R.O.P. to L.O.A. and from L.O.P. to R.O.A. The transverse positions are similarly overcorrected, i.e., R.O.T. to L.O.A. and L.O.T. to R.O.A. This rotation can be performed as soon as the cervix is sufficiently dilated to admit the whole hand. It was Pomeroy's custom to perform anterior rotation and then leave the case to nature.

Pomeroy and Aranow report excellent results from this procedure. I have personally performed the Pomeroy maneuver many times and I can attest to its efficacy.

After some experience with rotation I found that it was not necessary to rotate the shoulder; that the rotation of the head alone would safely effect the change from a posterior or transverse position to an anterior. The best results, however, are obtained when rotation of the head is done by minutely following the technic as worked out by Pomeroy in his shoulder rotation. I have tried rotation by ordinary methods and found that it is far inferior to the Pomeroy method. Manual rotation of the head when performed in a manner similar to Pomeroy's shoulder method will immeasurably facilitate rotation and will greatly lessen the complications and dangers of the persistent occiput posterior and transverse positions.

#### TECHNIC

Unless there is an emergency no interference is practiced until the cervix is fully dilated. If, after full dilatation, delivery is deemed advisable, the patient is anesthetized, preferably with ether, and placed in the lithotomy position. The bladder is emptied by catheter and the perineum is "ironed out" with tincture of green soap.

In R.O.P. and in R.O.T. the operator faces the patient's right thigh, bends both knees as much as is necessary, and acutely bends his body at the waist sharply to the left. He then inserts his whole right hand into the vagina and the forearm is pronated so that the thumb is below and

posterior and the other four fingers above and anterior to the fetal head. The operator then slowly assumes the erect posture and as he does so he supinates his forearm thus forcing the occiput to rotate 180 degrees in the case of occiput posterior and in either case converting the position into an L.O.A.



FIG. 1.—Showing first position of operator in effecting rotation.

In L.O.P. and in L.O.T. the operator faces the patient's left thigh, bends his knees as above, and acutely bends his body at the waist to the right. He inserts his whole left hand into the vagina and proceeds as above described, rotating the head into the R.O.A. position as he straightens his body and supinates his forearm.

After completion of the rotation, which rarely takes more than half a minute, a nurse or an assistant exerts pressure on the fundus until the forceps are applied. While advisable, this procedure is not essen-

tial. I have frequently performed rotation where no assistant or nurse was available, fundal pressure was not employed, and the head rarely rotated back to either its former or the corresponding anterior position. Should the head rotate back to or toward its former position, the maneuver is simply repeated. A cephalic application of the type of forceps to which the operator is accustomed is then made and delivery effected in the usual manner.

The contraindications to this procedure are appreciable contractions of pelvis and disproportion. In cases of this sort where vaginal delivery is considered reasonably possible I prefer internal podalic version.



Fig. 2.—Showing second position.

I have frequently displaced the head rather high while performing the maneuver, but since I perform rotation only in fairly normal pelvis I found that this high displacement made very little difference in the delivery. Whereas I would under no circumstances apply high forceps in contracted pelvis, I do not hesitate to do so in these cases. In some of these cases where the head was unduly displaced I performed podalic version from choice and not of necessity.

I have delivered 146 patients by this modified Pomeroy technic. I never failed to effect rotation. However, in a few cases, because of disproportion, I was unable to deliver by forceps after rotation. These patients I delivered by podalic version. These latter cases are not included among the 146 in this report.



TABULATION OF CASES			
PARA 0	PARA I	PARA II	PARA III
113	22	9	2
R.O.P.	R.O.T.	L.O.P.	L.O.T.
95	8	37	6

In one case the patient was allowed to deliver spontaneously after completion of the rotation. Two cases were delivered as posterior.

In six cases I was called after the attendants had unsuccessfully attempted delivery with forceps. In every case delivery was either easy or fairly easy after rotation. There were no maternal deaths.

There were three fetal deaths. In two of these cases I could hear no heart sounds when the family doctor called me to deliver the patients. In one case the labor had lasted four days, and in the other case labor had lasted over two days, and the doctor had made several attempts on different occasions to effect delivery with forceps. The third case was also one of prolonged labor, and the family doctor had unsuccessfully tried forceps delivery at the patient's home. The baby lived for one day after delivery. Death was in all probability due to cerebral hemorrhage. No autopsies could be obtained.

There were four cases of Erb's palsy. They were all of the mild variety and cleared up in a short time.

#### CONCLUSION

The 180 degree manual rotation of the occiput is one of the most efficient if not the most efficient method of treating persistent occipitoposterior or transverse positions.

#### REFERENCES

- (1) *Tweedy, E. H.*: Practical Obstetrics, London, Oxford University Press. (2) *Williams, J. W.*: Obstetrics, New York, 1930, D. Appleton-Century Company. (3) *Piper, E. B.*: In Curtis' Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Co. (4) *Caldwell, W. E., Moley, H. C., and D'Esopo, D. A.*: AM. J. OBST. & GYNEC. 28: 824, 1934. (5) *Aranow, H.*: New York J. Med. 26: 961, 1926.

1882 GRAND CONCOURSE

---

Ito, Sh.: Mastitis and Puerperal Psychosis, Jap. J. Obst. & Gynec. 17: 373, 1934.

Ito maintains that infection due to trauma during delivery often leads to puerperal psychosis. Other causes of puerperal psychosis are intense pruritus, carbuncles, mastitis, pneumonia, etc. The occurrence of puerperal psychosis following mastitis is rare and the author reports such a case. The psychosis disappeared shortly after the abscess was incised and drained. The patient has remained well. The most important immediate cause of the psychosis was the bacterial toxin from the breast abscess. Contributing factors were individual predisposition, the puerperium and fear, also pain and fever associated with the mastitis.

J. P. GREENHILL.

# THE RESULTS OF TREATMENT OF BENIGN LESIONS OF THE CERVIX UTERI

PENDLETON TOMPKINS, M.D., PHILADELPHIA, PA.

*(From the Gyneccean Hospital Institute of Gynecologic Research, and the Department of Gynecology, University of Pennsylvania)*

THE results of treatment of non-neoplastic diseases of the cervix uteri in the Hospital of the University of Pennsylvania are reported in this paper. The study is confined to three topics: (1) relief of leucorrhea, (2) conception subsequent to cervical repair, and (3) incidence of carcinoma following repair.

## SOURCE OF DATA

About 18 per cent of the patients admitted to the Hospital Service of the Department of Gynecology between 1899 and 1934 received treatment for cervical lesions. Of the 4,050 patients so treated, 18 per cent (741 patients) had malignant, and 82 per cent (3,309 patients), benign diseases of the cervix. The patients treated for carcinoma of the cervix have been reported upon by Norris<sup>1</sup> and by Keene and Kimbrough.<sup>2</sup> The present study of the benign lesions is based upon information gathered partly by follow-up examination but largely from questionnaires returned by 600 patients treated for cervical diseases in the twenty years from 1914 to 1934. Thirty-three per cent of 1,800 questionnaires were answered. (This is the usual return for questionnaire studies on this subject; Rawls<sup>3</sup> 30 per cent, Leonard<sup>4</sup> 32 per cent, Bullard<sup>5</sup> 38 per cent.) Of the 600 answers, 58 per cent were from ward and 42 per cent from private patients. The approximate proportions of all patients admitted to the department are 65 per cent ward and 35 per cent private. The files of the department contain recent information on eleven additional patients, making a total of 611 patients traced. The average age of the patients when treated was thirty-nine years, and when traced by questionnaire forty-seven years, making the average period of follow-up eight years.

## PURPOSE OF TREATMENT

The purpose of treatment of the cervix was (1) relief of abnormal discharge, (2) eradication of cervical infection, (3) anatomic restoration of the cervix. An additional consideration was the extirpation of potentially malignant tissue. The prophylactic effect of cervical surgery against subsequent carcinoma is of especial interest, as will appear below. Treatment of the cervix was not undertaken for the pur-

pose of relieving backache, abdominal pain, or dysmenorrhea (except that due to cervical obstruction). No patient in the present series who received treatment of the cervix alone was relieved of backache or abdominal pain. This observation supports Fulkerson's<sup>6</sup> opinion that uncomplicated cervicitis does not cause backache.

#### INDICATIONS FOR EACH TYPE OF TREATMENT

Since all the patients were admitted to the hospital, it was possible to undertake any operative treatment of the cervix which was indicated. Minor degrees of erosion, endocervicitis, and cystic cervicitis were treated by cauterization, usually under anesthesia. Occasionally, to save time in a case requiring extensive abdominal surgery, the cervix was treated by cauterization rather than by a more time-consuming method which might otherwise have been preferable.

Cervices presenting marked anatomic defects such as deep laceration and eversion, extensive endocervicitis or cystic changes, were treated by Sturmdorf's operation or by amputation. In recent years the Sturmdorf stitch has been used for covering the stump after amputation.

In general the operation of choice was that which promised to eradicate infection and to restore the cervical contours most effectively. The effect upon subsequent childbirth was a secondary consideration, for it was believed that the principal problem was improvement of an existing condition rather than provision for a future contingency. However, in treating patients in the childbearing age a minimum of cervical tissue was removed. In older women more extensive excision was practiced.

The 611 patients included in this study were operated upon by one of a staff of six men formerly headed by, and still influenced by, Dr. John G. Clark. Adherence to his principles has maintained in the present staff an exceptionally uniform system of treatment of cervical lesions, which may account, in part, for the uniformity of the results obtained.

#### EFFECTIVENESS OF VARIOUS METHODS IN THE TREATMENT OF LEUCORRHEA

By following up 171 patients treated in this clinic, Payne<sup>7</sup> found that all methods of treatment (cauterization, trachelorrhaphy, Sturmdorf operation and amputation) gave approximately the same percentage of relief from leucorrhea when the choice of treatment was governed by the considerations outlined above. He concluded that effective treatment of leucorrhea depends mainly upon the selection of a type of treatment appropriate to the individual case. Surgical judgment seemed to him of greater importance than surgical technique. The present study of 611 patients (including Payne's) supports his beliefs. Each of the four methods studied gave *relief* in approximately 84 per cent of patients so treated (Table I).

TABLE I. COMPARISON OF RESULTS OF DIFFERENT TREATMENTS FOR LEUCORRHEA (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL		TOTAL CURED OR IMPROVED	CURED	IMPROVED	NOT IMPROVED
	PATIENTS	PER CENT				
Cauterization	185	100	86%	80%	6%	14%
Trachelorrhaphy	90	100	83%	70%	13%	17%
Sturmdorf	135	100	84%	80%	4%	16%
Amputation	48	100	85%	83%	2%	15%
Final results from all methods of treatment	458*	100	84%	78%	6%	16%

\*None of these patients received gynecologic treatment, or conceived during the period of follow-up.

It will be noted that trachelorrhaphy gave the lowest percentage of *complete cures*, as might be expected of a procedure which does not remove all the infected endocervix. Moreover, trachelorrhaphy was the slowest treatment in effecting cure (Table II).

TABLE II. INTERVAL BETWEEN TREATMENT FOR LEUCORRHEA AND CURE (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)\*

	TOTAL		INTERVAL IN MONTHS			
	PATIENTS	PER CENT	0-1	2-3	4-11	12 AND OVER
Cauterization of the cervix	98	100	43%	35%	11%	11%
Trachelorrhaphy	41	100	32%	27%	21%	20%
Sturmdorf operation	63	100	48%	30%	11%	11%
Amputation of the cervix	23	100	35%	35%	13%	17%
All treatments	225	100	42%	32%	13%	13%

\*It will be noted that of those patients who were completely cured of leucorrhea, in three months, 78 per cent were cured by the cautery, 78 per cent by Sturmdorf, and 70 per cent by amputation but that, in the same period, trachelorrhaphy had accomplished a cure in only 59 per cent.

#### RESULTS IN THE TREATMENT OF LEUCORRHEA

Leucorrhea was present in 85 per cent of our 611 patients who required treatment of the cervix. (It was present in 74 per cent of Fulkerson's<sup>6</sup> series, 80 per cent of Sovak's,<sup>5</sup> and 85 per cent of Leonard's.<sup>4</sup>)

Payne's<sup>7</sup> studies in 1929 showed that approximately 96 per cent of 171 patients who had been treated for leucorrhea in this clinic were cured or improved. His follow-up period was one to five years, and the results he reported were as good as those published elsewhere. The present series shows 84 per cent of patients cured or improved. This percentage of relief of leucorrhea, which is lower than Payne's or most other authors' (Table III) may be accounted for by the longer period of follow-up in the present series (one to twenty years). During that period the early good results may have been modified by infection (gonococcus, trichomonas vaginalis), childbirth, prolapsus uteri, subsequent

operation, etc. Allowance has been made for these factors when known. Although approximately 15 per cent of patients who were treated for leucorrhea were not improved, this does not necessarily indicate a poor anatomic result, for Fulkerson<sup>6</sup> found that 14 per cent of patients whose cervixes had healed satisfactorily after repair still complained of leucorrhea.

Data from the present series are not available for a study of the causes of failure to cure leucorrhea.

TABLE III. RESULTS OF TREATMENT FOR LEUCORRHEA

AUTHOR	NUMBER OF PATIENTS TREATED	TOTAL CURED OR IMPROVED	PER CENT			
			CURED	IMPROVED	NOT IMPROVED	TOTAL
<i>Antiseptics and Caustics</i>						
Fulkerson <sup>6</sup>	423	82%	12	70	18	100
<i>Canterization of the Cervix</i>						
Fulkerson <sup>6</sup> (no anesthetic used)	524	98%	74	24	2	100
Matthews <sup>9</sup> (no anesthetic used)	226	100%	80	20	0	100
Matthews <sup>9</sup> (anesthetic used)	55	84%	51	33	16	100
Tompkins <sup>8</sup> (anesthetic usually used)	185	86%	80	6	14	100
<i>Trachelorrhaphy</i>						
Bullard <sup>5</sup>	50	74%	—	—	—	—
Rawls <sup>3</sup> (cervical repair only)	66	83%	44	39	17	100
Rawls <sup>3</sup> (cervical and vaginal repair)	35	72%	34	38	28	100
Leonard <sup>4</sup>	33	84%	42	42	16	100
Tompkins <sup>8</sup>	90	83%	70	13	17	100
<i>Sturmdorf Operation</i>						
Bullard <sup>5</sup>	53	92%	—	—	—	—
Burns <sup>10</sup>	92	97%	—	—	—	—
Wolfe <sup>11</sup>	130	97%	79	18	3	100
Sovak <sup>8</sup>	75	93%	88	5	7	100
Matthews <sup>12</sup>	200	92%	64	28	8	100
Matthews <sup>9</sup>	70	93%	70	23	7	100
Tompkins <sup>8</sup>	135	84%	80	4	16	100
<i>Amputation of the Cervix</i>						
Bullard <sup>5</sup> (high amputation)	39	100%	—	—	—	—
Bullard <sup>5</sup> (low amputation)	99	88%	—	—	—	—
Leonard <sup>13</sup>	109	93%	63	30	7	100
Rawls <sup>3</sup> (amputation only)	128	92%	61	31	8	100
Rawls <sup>3</sup> (amputation and vaginal repair)	77	90%	57	33	10	100
Tompkins <sup>8</sup>	48	85%	83	2	15	100

\*Data assembled for present report.

## CONCEPTION SUBSEQUENT TO TREATMENT OF THE CERVIX

It is the opinion of some gynecologists that conception is less likely to follow amputation than other cervical operations (Table IV). In our series approximately two-thirds of all patients who were likely to conceive did so regardless of the type of treatment of the cervix (Table V).

TABLE IV. PERCENTAGE OF PRESUMABLY FERTILE WOMEN WHO CONCEIVED SUBSEQUENT TO TREATMENT OF THE CERVIX

AUTHOR	LEONARD	RAWLS	SOVAK	BURNS
Length of follow-up	1-20 YEARS	1-5 YEARS	2-3 YEARS	2 YEARS
Number of presumably fertile women	101	149	54	65
Trachelorrhaphy	38%	42%	—	—
Sturmdorf operation	—	—	66%	22%
Amputation of the cervix	20%	28%	—	—

TABLE V. PREGNANCY SUBSEQUENT TO CERVICAL TREATMENT OF 256 WOMEN\* WHO HAD PREVIOUSLY BORN CHILDREN (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL		NOT PREGNANT SUBSEQUENTLY	PREGNANT SUBSEQUENTLY
	PATIENTS	PER CENT		
Cauterization of the cervix	75	100	37%	63%
Trachelorrhaphy	80	100	29%	71%
Sturmdorf operation	83	100	28%	72%
Amputation of the cervix	18	100	39%	61%
Pregnancy subsequent to all treatments	256	100	32%	68%

\*Widows, divorcees, women over forty, women not menstruating regularly, women treated by radium or surgical sterilization, not included.

When nulliparous married women were considered, it was found that approximately half of those who received no operative treatment except treatment of the cervix later conceived (Table VI).

From the data available it is not possible to determine whether cervical repairs, by producing stenosis, decrease the chance of subsequent con-

TABLE VI. PREGNANCY SUBSEQUENT TO CERVICAL TREATMENT OF 25 PRESUMABLY FERTILE\* MARRIED WOMEN WHO HAD NEVER BEEN PREGNANT (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL PATIENTS	NOT PREGNANT SUBSEQUENTLY	PREGNANT SUBSEQUENTLY
Cauterization of the cervix	22	9	13
Trachelorrhaphy	1	1	0
Sturmdorf operation	2	1	1
Total	25	11	14
	100%	44%	56%

\*Widows, divorcees, women over forty, women not menstruating regularly, women treated by radium or surgical sterilization not included.

ception. In the first place, many patients do not submit to repairs until their families are completed. Further, many patients are advised not to bear children after a plastic repair; and a few in whom repairs have been extensive, are warned that future pregnancy should be terminated by cesarean section. Therefore, as Rawls<sup>a</sup> pointed out, the voluntary sterility of women tends to increase after repair of the cervix.

The same factors also influence the incidence of voluntary abortion and miscarriage among women who become pregnant after repairs. Therefore we have made no attempt to study the effect of such treatment as regards predisposition to miscarriage.

Reliable information is not available for a study of dystocia and premature labor subsequent to cervical repair in this series of patients.

#### INCIDENCE OF CARCINOMA AFTER CERVICAL REPAIR

In studying the value of cauterization and other treatments of the cervix as prophylaxes against carcinoma, the closest scrutiny must be

TABLE VII. CARCINOMA SUBSEQUENT TO TREATMENT OF BENIGN LESIONS OF THE CERVIX (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	NUMBER OF PATIENTS	AVERAGE AGE WHEN TREATED	AVERAGE AGE WHEN FOLLOWED UP	AVERAGE FOLLOW-UP PERIOD	SUB- SEQUENT CERVICAL CARCINOMA
Cauterization	228	37.0	43.0	6.0 years	0
Trachelorrhaphy	116	34.5	44.5	10.0 years	1
Trachelorrhaphy and light cauterization	10	36.5	43.5	7.0 years	0
Sturmdorf operation	180	41.5	49.0	7.5 years	1
Amputation	77	44.5	55.0	10.5 years	0
Totals	611	39.0	47.0	8.0 years	2

This table is based upon a follow-up of 611 patients treated between 1914 and 1934. Attempts to trace 1,200 additional patients treated in the same period were unsuccessful, but none of them is known to have developed carcinoma of the cervix. The Sturmdorf operation and cauterization were not regularly employed until after 1920, which accounts for the shorter follow-up period in groups treated by these methods. The table shows the tendency to use the Sturmdorf operation or amputation in older patients.

Brief abstracts of the histories of the two patients who developed carcinoma are given:

CASE 1.—M. B., para iii, trachelorrhaphy at twenty years of age. No pathologic report on the tissue removed. Pelvic symptoms were relieved for twenty years. No pregnancy subsequent to cervical repair. At twenty-six a radical mastectomy was performed for scirrhus carcinoma (histologic diagnosis) in the Hospital of the University of Pennsylvania (Surgical Records 62: No. 8528). At the age of forty, metrorrhagia developed. Stage III cancer of the cervix was discovered. Biopsy showed epidermoid carcinoma (Gynecologic No. 14192).

CASE 2.—F. S., para iii, Sturmdorf operation at thirty-three years of age for leucorrhea. Microscopic examination of tissue removed showed no carcinoma. No subsequent pregnancy. The leucorrhea was not relieved. Total hysterectomy at thirty-eight years of age. No clinical evidence of carcinoma but routine histologic examination of the uterus showed epidermoid carcinoma in the cervical portion (Gynecologic No. 22966).

focused upon the favorable statistics which have previously been published. Attention should be directed to the percentage of patients followed, the length of the follow-up, and the average age of the patients. In evaluating the accumulated statistics of several authors, the student must be certain that there is no "overlapping" of the cases tabulated.

In the present study questionnaires were mailed to 1,800 patients treated in this clinic between 1914 and 1934 for benign lesions of the cervix. Microscopic examination of the tissue removed by cervical repair did not show carcinoma in any instance. Six hundred patients were traced by questionnaire. In addition eleven patients have recently reported to the department. Two of these patients have developed carcinoma of the cervix subsequent to cervical repair (Table VII). It should be noted that most of the patients listed in Table VII have not recently been examined, so that it is possible that some of them have cervical carcinoma at the present time without our knowledge.

#### SUMMARY

1. Six hundred and eleven patients treated for benign cervical lesions at the Hospital of the University of Pennsylvania between 1914 and 1934 were traced.

2. The methods of treatment were canterization, trachelorrhaphy, Sturmdorf operation and amputation. The indications for each are outlined.

3. Each method gave *relief* of leucorrhea in approximately 85 per cent of cases.

4. Trachelorrhaphy gave a lower percentage of *complete cure* of leucorrhea and effected cure more slowly than other methods.

5. Statistics from other clinics on the relief of leucorrhea have been tabulated for comparison.

6. Approximately 66 per cent of married women in the childbearing age who had previously borne children conceived after each type of cervical repair.

7. Approximately 50 per cent of married women in the childbearing age who had never been pregnant conceived after cervical repair.

8. The tendency of cervical repair to increase voluntary sterility and abortion is discussed.

9. Two patients among 611 who were traced after the repair of benign lesions of the cervix subsequently developed cervical carcinoma.

#### CONCLUSIONS

1. The most important factor in the relief of leucorrhea due to cervicitis is the selection of a type of treatment suitable to the individual case. Approximately 85 per cent of patients will be *relieved* of leucorrhea if the choice of treatment is based upon the indications outlined.



2. In general, trachelorrhaphy cannot be recommended as a satisfactory procedure when the principal object of treatment is *complete cure* of leucorrhea.

3. The possibility of producing cervical stenosis which will interfere with conception should not influence the choice of treatment for benign lesions of the cervix.

#### REFERENCES

- (1) Norris, C. C.: Surg. Gynec. Obst. 58: 458, 1934. (2) Keene, F. E., and Kimbrough, R. A., Jr.: AM. J. OBST. & GYNEC. 23: 838, 1932. (3) Rawls, R. M.: AM. J. OBST. & GYNEC. 3: 1, 1922. (4) Leonard, V. N.: Surg. Gynec. Obst. 18: 35, 1914. (5) Bullard, E. A.: AM. J. OBST. & GYNEC. 27: 668, 1934. (6) Fulkerson, L. L.: AM. J. OBST. & GYNEC. 12: 374, 1926. (7) Payne, F. L.: AM. J. OBST. & GYNEC. 17: 841, 1929. (8) Sovak, F. W.: AM. J. OBST. & GYNEC. 15: 686, 1928. (9) Matthews, H. B.: J. A. M. A. 87: 1802, 1926. (10) Burns, J. W.: Lancet 2: 806, 1925. (11) Wolfe, S. S.: AM. J. OBST. & GYNEC. 24: 87, 1932. (12) Matthews, H. B.: Surg. Gynec. Obst. 32: 249, 1921. (13) Leonard, V. N.: Surg. Gynec. Obst. 16: 390, 1913.

### COMPLICATIONS FOLLOWING CAUTERIZATION OF THE CERVIX UTERI

DOUGLAS CANNELL, M.D., AND MARION DOUGLASS, M.D., F.A.C.S.,  
CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, Western Reserve University School of Medicine and the Lakeside Hospital)

THE use of the electrocautery in the treatment of diseases of the cervix uteri is far from being a harmless procedure and may produce serious infection. The feeling has arisen, unfortunately, that no complications need be feared in routine use of the cautery. The application of the cautery in the treatment of endocervicitis and other lesions of the cervix was first suggested by Byrne in 1892, and has become an exceedingly common procedure. The method, originated in its present form by Hunner in 1906, has become most convenient and popular in the management of even very severe erosions and eversion.

The ease with which the method may be applied and the excellent results obtained almost painlessly in office practice or under anesthesia in the operating room, almost universally, has had the effect of minimizing any apprehension on the part of those employing cautery treatment. Abnormal epithelium is destroyed, deep infection is checked, followed in the majority of cases by epithelialization of the cervix and complete cure of the lesion, without surgical operation or prolonged treatment.

There are many modifications of cautery tips, viz., the nasal cautery suggested by Dickinson, the Cherry, Ende, and Hyams types. The electrocautery is very effective in treating cysts of endocervicitis, cervical polyps, and all types of erosions. Curtis advises against the heavy duty or Paquelin cautery. Masson and Parsons have reported great effectiveness of the cautery in all types of leucorrhea in which infection of the cervix is the etiologic factor.<sup>1</sup> Holden has described in detail the method of treating high cysts with marked dilatation of the cervical canal effectively with cautery.<sup>2</sup> Its use is advocated also in the treatment of obstinate gonorrheal infections where it may be of service in destroying the primary stubborn foci which produce persistent reinfection, and its use is suggested (Curtis) between attacks of acute salpingitis to prevent subsequent exacerbations by eliminating persistent foci.<sup>3</sup> The contraindications and dangers of cautery treatment, however, have not been sufficiently emphasized. Curtis recently has stated "reticence in discussing unfavorable results has perhaps tended to conceal the *true incidence of complicating cellulitis*; nearly all with whom I have discussed this subject state that they have had cases of pelvic cellulitis in patients subjected to endocervical cauterization." He emphasizes also the important observation that the danger is augmented in cases of displacement where there is interference with good mechanical drainage from the uterus and necrotic infected material stagnates within the uterine canal. Masson and Parsons report three cases of pelvic abscesses occurring in their series of cases.

We have observed recently a number of complications following cauterization, three of which are reported here.

The complications occurring in our hands have followed cauterizations after the heavy duty cautery, or the Postcautery in office practice. Very light surface cauterization with the finer types of cautery is definitely advisable but is less effectual.

CASE 1.—This patient, a white woman of twenty-six, para 0, was admitted to the Lakeside Hospital, July 1, 1933, complaining of profuse and irregular menstruation of several months' duration. Pelvic examination revealed nothing of note at that time except a marked erosion of the cervix. Smears were negative. A diagnostic curettage was performed and the cervix was cauterized. This patient was readmitted two weeks later complaining of severe bilateral abdominal pain, nausea, and vomiting. There was moderate fever and irregular spotting. A definite mass could be felt on the right side, and there was marked bilateral tenderness, and a tubal pregnancy being suspected, laparotomy was performed after three days' observation. Laboratory findings were consistent with acute salpingitis. Old blood was obtained on culdesac needle puncture. The gross findings at operation were those of acute salpingitis, both tubes being sealed off and swollen markedly. There were a few old clots in the culdesac. Bilateral salpingectomy was performed. Microscopic examination revealed an ectopic gestation in the right tube, which was adherent to the ovary, and subacute bilateral salpingitis. The postoperative course was uneventful and patient was discharged July 30, 1933, convalescing satisfactorily. The ectopic pregnancy was incidental obviously but the acute tubal inflammation seemed definitely to have been initiated by the cauterization.

CASE 2.—This patient was a twenty-one-year-old nullipara, who was admitted to Lakeside Hospital, March 21, 1933, complaining of backache and pain in the left side, with vaginal discharge of three months' duration. The past history was negative except for appendectomy and oophorectomy in 1931 (presumably an attack

of salpingitis). Family history and marital history otherwise essentially negative. Menstrual history negative except for an abortion in 1932, without infection, as far as could be ascertained from the history. . . .

Physical examination was not remarkable. Pelvic examination showed a marital outlet in good condition. The cervix was markedly eroded, the uterus was in deep midposition, only fairly movable, and there were no lateral masses made out. The cervix was dilated. It was markedly hypertrophied and contained numerous large infected nabothian follicles. The cervix was cauterized thoroughly under anesthesia and a Smith-Hodge pessary was inserted to give the uterus a better position for drainage. The patient was discharged on her second postoperative day without an elevation of temperature. One week later she complained of soreness in both lower quadrants, which persisted until her admission to the hospital April 12, 1933. Physical examination at this time revealed a moderately ill white woman with the usual signs of toxemia. There was marked tenderness in both lower quadrants with some spasticity. Pelvic examination revealed a cervix still acutely inflamed from cauterization, and the uterus was small and anterior; there was a large mass in the culdesac. Her temperature was 38.8° C., pulse 90, and respirations 22. The white blood count was 7,650. Sedimentation tests showed moderate activity.

A posterior colpotomy was done on her first hospital day and 500 c.c. of foul-smelling pus evacuated. Temperature immediately fell to normal and she was discharged on her seventh postoperative day in good condition. It is impossible to say whether the cauterization lighted up a latent infection persisting, perhaps, from the abortion or an old salpingitis, or whether the abscess was metastatic from the badly infected cervix.

CASE 3.—This patient was admitted to Lakeside Hospital, March 13, 1934, complaining of constant vaginal discharge with lower abdominal pain since October, 1933, at which time she had had an induced abortion. She was suspected of having an ectopic pregnancy as she complained of severe abdominal pain and faintness shortly before her admission to the hospital. Her past two periods had been prolonged but were otherwise normal. Aschheim-Zondek test was negative. Smears from the cervix were negative.

Her anamnesis was unessential. Physical examination was essentially negative except for the pelvis which showed normal external genitalia, a markedly eroded cervix, and a fundus in retroversion pulled slightly to the left. No abnormal lateral masses were felt. Laboratory findings revealed nothing of note. On her second hospital day a dilatation and curettage were done. The scrapings showed interval endometrium. The cervix was cauterized, and the fundus was replaced and held anteriorly by a Smith-Hodge pessary. She was discharged March 15, 1934 in good condition.

She returned to the dispensary March 21, 1934 complaining of abdominal pain and soreness, which grew worse with exercise. Pelvic examination was negative except for some sloughing of the cervix and lower abdominal tenderness. She returned again April 4, 1934 with similar complaints and more obvious physical findings with marked tenderness in both fornices, which was more marked on motion of the cervix. She returned again April 13, 1934, complaining of much more pain and vaginal bleeding. She was not examined at this time. She made five subsequent visits to the dispensary, the last, June 27, 1934, when she complained at this time of severe dysmenorrhea, and moderate backache with profuse bleeding at her last period, at which time the fundus was in mid- to anterior position, bilateral masses were present in the fornices, the larger of which was in the left fornix and measured 5 by 7 cm.

in diameter, and both fornices were exquisitely tender. She was still undergoing Elliott treatment three months later with marked regression of her cellulitis. The immediate response in the form of a pelvic flare-up strongly suggests that a part was played in its etiology by the cauterization.

The occurrence of widespread pelvic infections following cauterization is evidently much more frequent than is commonly supposed. The presence of a latent gonorrheal infection of the cervix should be carefully eliminated wherever possible. Patients with a history of infected abortion, especially of recent occurrence, should be dealt with most cautiously as subjects for cervical cauterization especially with the heavy duty or Paquelin cautery. Since these cases, we have had under observation recently an instance of pelvic inflammatory disease, apparently immediately initiated by office cauterization for erosion of the cervix in a patient with adherent retroversion of the uterus and one-child sterility of seven years' duration. This patient had had a number of negative smears and had no local stigmas of gonorrhea. These cases suggest that the cautery should be employed with extreme care and circumspection and with the knowledge that severe cellulitis may result occasionally as a complication.

#### REFERENCES

- (1) *Masson, J. C., and Parsons, E.*: AM. J. OBST. & GYNEC. 16: 348, 1928. (2) *Holden, F. C.*: AM. J. OBST. & GYNEC. 16: 624, 1928. (3) *Curtis, A.*: Textbook of Gynecology, Philadelphia, 1930, W. B. Saunders Co.

---

*Naeslund, J.*: The Fibrinogen Content of the Blood of Newborn Babies, Acta obst. et gynec. Scandinav. 14: 143, 1934.

The amount of fibrinogen in the blood of healthy children at birth seems to be low; it then rises rapidly to something above 2 per cent after a week. This rise in the first few days after birth cannot be occasioned by loss of water alone, as the amount of serum albumin, and consequently of water also, seems to undergo no change.

In the sick children which the author examined, particularly in those exhibiting an increased tendency to bleeding, this rise in the amount of fibrinogen in the blood seemed to be absent, the values generally remaining lower than in healthy children of corresponding age. Also the power of coagulation of the blood was considerably lowered in these children. The low amount of fibrinogen and the lowered power of coagulation in the blood of children suffering from hemophilia neonatorum temporaria probably are to be regarded as causative of this condition, although other factors, as for example a change in the amount of calcium and fluorid contained in the blood, and also its degree of oxygenation, may play a certain part. After transfusion of blood the amount of fibrinogen is increased, and also the power of coagulation of the blood, which circumstance may possibly explain the favorable effect of blood transfusion on children with a heightened tendency to bleeding.

J. P. GREENHILL.

## THE SEX PREDICTION TEST OF DORN AND SUGARMAN

W. T. POMMERENKE, M.D., AND W. C. ROGERS, M.D., ROCHESTER, N. Y.  
(*Department of Obstetrics and Gynecology, Strong Memorial Hospital, University of Rochester School of Medicine and Dentistry*)

DORN AND SUGARMAN, in 1931, while investigating the possibility of utilizing male rabbits for the Aeschheim-Zondek method of diagnosing pregnancy, observed that singular differences in the testicular response became apparent following the injection of urine from pregnant women. These differences were ascribed to hormones dependent on the sex of the unborn child. By injecting immature rabbits with urine of women in the fifth to tenth months of pregnancy, these authors were able to correctly foretell the sex of the unborn child in 80 out of 85 cases. Urine from women carrying female children was found to stimulate the testes to precocious development as evidenced by grossly recognizable enlargement and congestion, as well as by microscopic signs of accelerated spermatogenesis. This stimulation was not observed when the injected urine came from women bearing male children. The importance of using suitable test animals was emphasized by these authors. For satisfactory results, it was found that the testes of the rabbits must already be through the inguinal rings, but not yet in the scrotum. In the event that the testes had not yet descended into the canal, they would not react to the injection, presumably due to their immaturity. On the other hand, after the testes had reached the scrotum, spermatogenesis had already been so well established that no further response could be elicited. These authors found that a relationship exists between the stage of descent of the testes and the development of spermatogenesis. This fact, according to them, obviates the need for controls. In 1933 Curphey and Romer described a spermatogenic factor in the urine of pregnant women, but this factor was apparently unrelated to the sex of the unborn child. They used a pure strain of rabbits and concluded that the anatomic position of the testis at the time of the injection of the urine of pregnancy appeared to play no part in testicular stimulation. By substituting the immature white rat for the rabbit, Daily, in 1934, was not able to demonstrate the stimulating action of the urine of pregnant women on the process of spermatogenesis, as read by the appearance of sperm heads in the tubules.

Our interest in the report of Dorn and Sugarman needs no comment. Wishing to gain familiarity with their methods and hoping that the utilization of this test would aid in solving the cauled secret of sex before birth, the following experiments were undertaken.

## METHODS

Male rabbits of known age and weight served as test animals. Note was made of the position of the testes with reference to their degree of descent. Urine, usually 10 c.c. in amount, coming from women in the latter months of pregnancy, was injected into the marginal ear veins. After forty-eight hours, or as otherwise specified in Table I, one testis was removed. In a few instances the second testis was also subsequently removed. The extirpated testis was carefully examined in the gross for evidence of enlargement, congestion, or engorgement of the surface vessels. The midportion of the testis was fixed in Zenker's solution, mounted in paraffin, sectioned at a thickness of 7 microns, and stained with hematoxylin and eosin. In the microscopic study, attention was directed to the degree of vascularity and cellular proliferation of the tubules. The stage of spermatogenesis, indicated by the formation of spermatogonia, spermatocytes, spermatids, and spermatozoa, was also noted. Preliminary observations impressed us with our inability to positively distinguish any appreciable or constant difference in the external appearance of the testes as the result of the injections of urine from women bearing male or female children. These conclusions were sometimes reached in the face of actual knowledge of the sex of the child, since the injected urine had been frequently furnished by women admitted to the hospital just prior to delivery. In every case, to evaluate properly the results of microscopic examination, sections of testes of healthy litter mates of similar size and stage of testicular descent, and which had been kept under the same environmental conditions were used for control. After having made a prediction of sex on the basis of the microscopic picture, using the criteria established by Dorn and Sugarman, this diagnosis was compared with the verified diagnosis. This served as a check on our observations and inferences. Finally, and without knowledge of the child's sex, the entire collection of slides was reexamined, and in this presentation, the criterion for the prediction of sex lay in the interpretation of the final microscopic examination of the testis. If on comparison with the control, the experimental section showed unmistakable evidence of accelerated spermatogenesis, the prediction of a female child was made. If, however, no appreciable change was apparent, a male child was foretold.

## OBSERVATIONS

After numerous observations, we were able to estimate the approximate age of the rabbit and the degree of descent of the testis by the microscopic appearance of the section. The immature testis is small and the individual tubules are lined only by one or two thin layers of cells. The more mature testis is much larger and in its tubules are seen deep layers of proliferating cells ranging from spermatogonia to spermatids and spermatozoa. One must, however, stress the existence of variations in degree of development of the different tubules even within one given section, particularly in those sections showing beginning spermatogenesis. In these cases we learned the hazard of venturing an opinion as to the exact stage of development of the testis on the basis of appearance of a single microscopic field. Here and there one may see small tubules containing only a single layer of cells at their peripheries. Elsewhere other tubules in the same section may show active proliferation with formation of spermatocytes and spermatids. The entire cross-section of the testis rather than any one microscopic field must be compared with the control section before reaching a conclusion as to any stimulating effect attributed to the injection.

The findings of our study are summarized in Table I. Forty-three tests are reported. There was no exclusion of cases except two instances in which it was not

TABLE I. INJECTION OF URINE FROM PREGNANT WOMEN INTO MALE RABBITS, WITH INTERPRETATION OF RESULTS

	TEST	RABBIT		POSITION OF TESTIS	URINE INJECTED C.C.	INTERVAL BETWEEN INJ. AND EXAM. HOURS	SEX OF CHILD		
		AGE WK.	WT. GM.				MALE		FEMALE PREDICTION
							PREDICTION		
A	1	11	1350	Canal	10	48	Correct	Correct	
	2	14	1020	Canal	10	48	Incorrect		
	3	16	1700	Scrotum	10	48	Correct		
B	4	9	810	Canal	15	24 & 48	Incorrect	Incorrect Incorrect Incorrect Incorrect Incorrect Incorrect	
	5	11	780	Canal	10	96	Correct		
	6	11	1390	Canal	10	48	Incorrect		
	7	11½	1600	Canal	10	48	Correct		
	8	11½	1700	Canal	5	48	Correct		
	9	16	1700	Scrotum	10	48	Correct		
	10	14	2040	Scrotum	10	48	Correct		
	11	16½	2160	Scrotum	10	48	Correct		
	12	7	1100	Canal	10	48	Correct		
	13	7	1210	Canal	10	48	Correct		
	14	11	890	Canal	10	72	Correct		
C	15	8	990	Canal	10	50 & 264	Correct†	Incorrect*	
	16	8	1350	Canal	10	48	Correct		
	17	11½	1620	Canal	10	48	Correct		
	18	11½	1650	Scrotum	10	48	Incorrect		
	19	12	1500	Canal	10	48	Correct		
	20	15	1370	Scrotum	10	48	Correct		
	21	16	2540	Scrotum	10	48	Correct		
	22	12½	2180	Scrotum	10	48	Correct		
	23	16½	2470	Scrotum	10	48	Correct		

TABLE I.—CONT'D

TEST	RABBIT AGE WK.	RABBIT WT. GMC.	POSITION OF TESTIS	URINE INJECTED C.C.	INTERVAL BETWEEN INJ. AND EXAM. HOURS	SEX OF CHILD	
						MALE PREDICTION	FEMALE PREDICTION
24	7	1100	Canal	10	48	Correct	Correct
25	8	680	Canal	10	48	Correct	
26	8	820	Canal	10	48	Correct	
27	8	900	Canal	10	48	Correct	
28	8	1100	Canal	10	48	Correct	
29	8	1100	Canal	10	50	Correct	
30	9	800	Canal	15	24 & 48		Incorrect
31	9	945	Canal	10	48		Incorrect
32	9	940	Canal	10	48	Correct	
33	9	990	Canal	10	48		Incorrect†
34	9	1140	Canal	10	48		Incorrect
35	9	1300	Canal	10	48		Incorrect
36	10	980	Canal	19	24 & 48		Incorrect
37	10	1400	Canal	10	48	Correct	Correct
38	10	1510	Canal	15	24 & 48		
39	11	880	Canal	10	96	Correct	
40	11	1400	Canal	10	48	Correct	
41	11	1590	Canal	10	48		Incorrect
42	11	1600	Canal	10	48	Correct	
43	12½	1320	Scrotum	10	48	Incorrect	

\*Anencephalic monster.

†Female twins.

‡Male twins.



possible to learn the sex of the child because the patient subsequently failed to return to the clinic. It will be noted that most of the rabbits were in the stage of development recommended by Dorn and Sugarman, viz, they were nine to twelve weeks of age and their testes were situated in the canals. Younger and older age groups are also represented. On inspection of the table, it is apparent that one cannot group the animals according to age and directly relate such grouping to weight and position of the testes. In Group A, using rabbits of different ages and weights but with testes in a comparable position, one correct and one incorrect diagnosis of sex was made with urine of two women carrying male children in the fifth month of pregnancy. In Test 3 the testes had already reached the scrotum, but there was evidence of advanced spermatogenesis, hence the correct prediction of a female child. In the group of rabbits (Group B in Table I) receiving injections of urine from women in the seventh month of pregnancy, the correct prediction of sex was made in one of five tests in those cases in which the testes were in the canals. In those cases in which the testes already were in the scrotum, one correct and two incorrect predictions were made. Twelve cases are represented in Group C. Urine from women in the eighth month of pregnancy was injected. In only one case, Test 18, of the male pregnancies was there evidence of increased spermatogenesis on comparison with the control. Here the testes had already reached the scrotum, but the increased spermatogenesis caused us to make the incorrect diagnosis of a female child. The sex of a set of identical twins was correctly foretold. The sex of a female anencephalic monster was wrongly predicted. Urine from two women bearing female children was injected into rabbits whose testes had already reached the scrotum (Tests 22 and 23). In the former test there was no increased spermatogenesis, but in the latter test increased cellular proliferation led to the correct diagnosis of sex. In Group D 20 tests were performed on urine from women in the ninth month of pregnancy, most of the specimens of urine having been collected after the patients had been admitted to the hospital shortly before delivery. Tests 29 and 32 were on the urine of the same woman, different rabbits however being used. In each case the sex of the child was correctly predicted. In another duplicate series, Tests 36 and 38, respectively, the spermatogenic response was positive in one case and negative in the other. Of the 11 "male" specimens, 1 showed a false positive reaction. Of the 9 "female" specimens, 2 were associated with increased spermatogenesis, whereas the remaining 7, including a set of identical female twins, showed no appreciable change. Summarizing the various groups, it is noted that 5 out of the 26 specimens of urine of male-bearing gravida gave false positive reactions. Thirteen out of 17 specimens of urine from female-bearing gravida gave false negative responses.

#### COMMENT

Our series is admittedly too small for the basis of any but tentative conclusions. We must assert in the light of our present knowledge the jeopardy of formulating opinions as to the specific effect of the injection of the urine of pregnancy on the testis. The question of dosage, the interval between the injection and time of examination, and the variations in degree of response are all important matters to be solved. Strict accuracy in reading the end-point is difficult, and different observers might find reasons for disagreement. The suitability even of a litter mate as a control has not been established. One observation, however, appears deserving of mention. Of 26 rabbits which received injections

of urine from women pregnant with male children, 5 (19.2 per cent) showed increased proliferation of the germinal epithelium in the seminiferous tubules. Of the 17 rabbits which received urine from women carrying female children, 4 (23.5 per cent) showed similar accelerated spermatogenesis. Just what significance this observation may have, we are not prepared to state. More study will be required to clarify this point and to establish a causal relationship between the injection of any particular constituent of the urine with any particular response of the testis. We were, however, unable to correlate the spermatogenic manifestation with the sex of the unborn child. In this respect our findings correspond to those of Curphey and Romer.

#### SUMMARY

Urine from women in the latter months of pregnancy was injected into pubescent male rabbits whose testes were subsequently examined for evidence of spermatogenesis and compared with the testes of litter mate controls.

Testes of 9 of the 43 rabbits injected showed evidence of accelerated spermatogenesis.

These 9 cases were almost equally divided (19.2 per cent and 23.5 per cent) between the animals which had been injected with urine from male-bearing and female-bearing women, respectively.

We were unable to correlate these changes with the sex of the unborn child.

#### REFERENCES

- Curphey, T. J., and Romer, A. S.: J. A. M. A. 101: 1630, 1933. Daily, E. F.: AM. J. ONST. & GYNEC. 27: 721, 1934. Dorn, J. H., and Sugarman, E. I.: J. A. M. A. 99: 1659, 1932.

---

v. Fekete, A.: Premenstrual Elevation of Temperature, Monatschr. f. Geburtsh. u. Gynäk. 99: 29, 1935.

The investigations of v. Fekete have revealed that even in completely healthy women there is a slight premenstrual elevation of temperature which subsides when the woman lies down. There is a slight but definite rise in temperature during the few days before the menstrual flow begins and also during the early months of pregnancy. Frequently these slight fevers are accompanied by uncomfortable sensations such as restlessness, a tired feeling, drowsiness, and general malaise. In such cases if no pathologic condition can be found to account for the fever, we may assume that the elevation is due to an increase in the function of the anterior pituitary gland. This disturbance in turn is caused by a relative insufficiency in the amount of folliculin. When the slight fever is associated with disagreeable symptoms, Fekete recommends the administration of repeated doses of estrogenic substance.

J. P. GREENHILL

## PREGNANCY COMPLICATING CARDIAC DISEASE

ISIDORE DAICHMAN, M.D., AND GEORGE KORNFELD, M.D., BROOKLYN, N. Y.

*(From the Obstetric Service of the Jewish Hospital)*

THIS paper is advisedly entitled "Pregnancy Complicating Cardiac Disease" because we wish to emphasize the cardiac status rather than the pregnancy. We should look upon these women as cardiac patients who have to bear the burden of a pregnancy, rather than pregnant women who have cardiac disease. This point of view will stress the importance of treating the cardiac disease first and the pregnancy afterward. A review of the literature of the past ten years shows a definite trend for closer cooperation between the cardiologist and the obstetrician, with the result that the pregnant cardiac patient is today getting better and more intelligent care than she did in the past. Most good maternity hospitals either have a cardiologist attached to their prenatal clinic, or the patient is referred from the prenatal to the cardiac clinic as soon as the heart lesion is discovered, and for the rest of her pregnancy she is watched and studied by both.

From 1924 to 1934 there were 22,100 women delivered at our hospital. Of these there were 205 with definite cardiac disease who were three or more months pregnant. This study does not include some twenty-five patients who had a therapeutic abortion done for cardiac disease in the early weeks of pregnancy. Most of the ward cases in this study were referred from the prenatal to the cardiac clinic as soon as the heart lesion was discovered. They continued to attend both clinics at frequent intervals and when admitted to the hospital for observation or in labor, they were frequently cared for by both the obstetrician and the cardiologist. Many of the private patients who showed evidence of cardiac distress while in the hospital were also seen by a cardiologist.

Most of our patients had a definite history of chorea or rheumatic fever. A few gave a history of a preceding pneumonia. One was due to syphilis (aortitis) and one was a congenital cardiac (pulmonary stenosis). The ages varied from nineteen to forty years. There were 111 primiparas and 94 multiparas. Of 205 cases, 85 had mitral stenosis alone, 90 had a double mitral lesion, 12 had a double mitral and an aortic lesion, 10 had mitral insufficiency, 1 had mitral stenosis and aortic insufficiency, 1 had mitral and aortic insufficiency, 4 had chronic myocarditis, one had congenital pulmonary stenosis, and one had syphilitic aortitis. Thus 91.7 per cent had mitral stenosis, either alone or combined with aortic disease. It is generally stated that about 90 per cent of pregnant cardiac patients have mitral stenosis.

Frequent references are made in the literature to the fact that cardiac patients often go into labor prematurely, have fairly short labors, and give birth to small babies. In our series, 34 or 16.3 per cent went into premature labor. The average weight of the babies was 6 pounds 12 ounces, a few ounces less than normal. The average duration of labor in 82 primiparas was 20.5 hours, considerably longer than normal. This is explained by the fact that there were 18 primiparas who had labors from twenty-four to seventy-two hours. The average duration of labor in 63 multiparas was 8.3 hours, a normal figure.

In classifying our pregnant cardiac patients we used the groupings advocated by the New York Heart Association and Dr. H. E. B. Pardee. We realize that the division of cases into Classes I, II A, II B, and III, is more or less arbitrary and has its limitations, yet we found it very helpful in studying the results obtained in each group. Class I consists of cases with perfect compensation, Class II A of those with fairly good compensation, II B cases are moderately decompensated, while those in Group III are badly decompensated.

The management of the pregnant cardiac patient consisted in limiting her activities in selected cases, rest in bed when necessary, the frequent use of mild sedatives, and admission to the hospital on the first signs or symptoms of cardiac embarrassment. About 30 per cent of our patients showed some signs of cardiac decompensation during pregnancy. Most of them belonged to Groups II B and III and a few to II A. Quite a number of patients were hospitalized for rest and study or for treatment for several weeks before the onset of labor or before the pregnancy was interrupted. These patients must have their cardiac condition treated as if no pregnancy existed. If the pregnancy is to be terminated, the heart is allowed to become well compensated before anything is done. Corwin, Herrick, Valentine, and Wilson have laid down the formula: "Cardiac decompensation plus forcible delivery equals death." Generally speaking, this is quite correct. These authors further state: "No attempt should be made to induce labor in a badly decompensated heart. Without delivery, the patient may die; with forcible delivery, she will almost surely perish."

Of those patients admitted in labor, the majority were given one or more doses of morphine or morphine and scopolamine as soon as possible, and the second stage was shortened by the frequent use of forceps. There were a good many patients belonging to Groups II B and III, who either had a rapid pulse and increased respirations or actually broke their compensation during the labor or immediately after delivery. During labor, the pulse and respirations are the most valuable guides we have as to the way the myocardium is behaving, because an increase in these is usually the forerunner of heart failure. While a great many of

the forceps were applied prophylactically, some were done because of an increase in pulse and respirations.

#### METHOD OF DELIVERY:

Spontaneous	65
Forceps	93
Version and extraction	6
Breech extraction	4
Abdominal hysterotomy and sterilization	4
Cesarean section without sterilization	8
Cesarean section with sterilization	22
Died undelivered	3
Induction by rupturing membranes	2
Induction with bag	1

With the exception of a few that were made under local infiltration, almost all of the vaginal deliveries were made under open drop ether anesthesia.

The cases handled by the abdominal route were 34 in number. Four patients had an abdominal hysterotomy and sterilization (1 at three months, 3 at four to four and one-half months) while 30 had a classical section done between the seventh and ninth months of pregnancy. Of the 30 sections, 22 patients were sterilized either by some form of tubal ligation or excision of the cornual ends of the tubes. There was one post-operative death due to a bronchopneumonia on the twenty-second day. The maternal mortality for the 34 cases was 2.9 per cent. Half of the 34 cases, or 50 per cent, had a temperature for an average of eight days. Five had wound infections, 4 had upper respiratory infections, 2 had pelvic peritonitis, 3 had phlebitis, and 2 had endometritis with foul lochia.

As regards cesarean section in pregnant cardiac patients, we feel rather strongly that it should be performed more frequently than at present because abdominal delivery under local infiltration will put the least strain on the myocardium of a certain group of cases. To be specific:

a. Cesarean section and sterilization should be done in patients who have had one or more breaks in compensation; also in patients showing evidence of myocardial damage or a severe aortic lesion, regardless into what group the case falls.

b. Cesarean section without sterilization should be done for cardiac patients who have either a borderline or truly contracted pelvis, a progressive toxemia, and for those patients who make no progress after ten to twelve hours of good labor.

In our group of 34 abdominal deliveries, 5 had a contracted pelvis, 2 had preeclampsia, 1 had no progress after thirty hours of labor, and several had electrocardiographic evidence of myocardial damage, although fairly well compensated. Four belonged to Group I, 12 to Group II A, 15 to Group II B, and 3 to Group III. Twenty were done under ether and 14 under local infiltration preceded by morphine, either

alone or with scopolamine. We believe that local anesthesia preceded by morphine and scopolamine is the ideal anesthetic for pregnant cardiac patients to be delivered abdominally, although Hamilton and Kellogg express a distinct preference for ether because they believe it to be safer, quicker, and nonexciting. About half of the patients who were sectioned were hospitalized for a variable period of time prior to operation, either for rest or for treatment. It is a mistake to operate upon a patient with a decompensated heart. This cannot be overemphasized. We also believe it inadvisable to wait for viability in patients who have been badly decompensated.

We found it convenient to divide our cases into the groups referred to previously, and in so doing, we were able to study and compare the results obtained in each group. Table I shows at a glance that as we proceed from one group to the next, the number of cardiac failures during or after labor and the number of deaths increases rather markedly.

TABLE I

GROUP	NO. OF CASES	RAPID PULSE DURING LABOR OR P. P.	FAILURE DURING LABOR OR IMMEDIATELY P. P.	DEATHS	PER CENT	CAUSE OF DEATH
I Well compensated	129	3	—	1	0.73	Subacute bact. endocarditis twenty-second day
II A Fairly well compensated	29	4	4	0	0.0	—
II B Moderately decompensated	29	—	11	4	13.7	(1) Pulmonary embolus, thirteenth day (1) Bronchopneumonia, twenty-second day (1) Subacute bact. endocarditis, eighteenth day (1) Heart failure, tenth day
III Badly decompensated	18	—	16	5	27.7	(3) Heart failure, undelivered (1) Heart failure, sixth day (1) Heart failure, tenth day
Totals	205			10	4.87	

Thus of 205 patients, 10 died, giving a maternal mortality of 4.87 per cent. In the literature, the mortality varies from 5 per cent to 10 per cent but is more often nearer 5 per cent. Reid, in a statistical analysis of the literature on pregnant cardiac patients, mentions 839

reported cases with a mortality of 5.1 per cent. From Table I it is apparent that the greatest trouble is encountered in Groups II B and III. These groups are responsible for 90 per cent of the failures during labor and also for 90 per cent of the deaths. This table illustrates the value of the groupings I, II A, II B, III from the point of view of prognosis.

Of the three patients who died undelivered, one was an ambulance patient who had never had prenatal care; patient was admitted in extremis and died in twelve hours. The other two were private patients admitted in acute decompensation, and in spite of very vigorous treatment, one died on the third day and the other on the fifth day after admission.

Twenty-two of our patients came back to the hospital either with another pregnancy or for medical care of their cardiac condition. The study of the records of this small group of cases is very instructive. These patients were seen from one to six years after a previous delivery. Of 11 patients who were originally in Group I, 3 were worse. Of 7 in Group II A, 1 died of heart failure within two years of her delivery, and 5 others were distinctly worse. Of 2 cases originally in Group II B, 1 was unchanged, while the other died of heart failure eighteen months after delivery. Thus, of 22 cases on which we had a follow-up, 3 patients were dead in two years, 8 were worse, and 11 unchanged as far as the cardiac status was concerned.

Scott and Henderson from a study of 56 autopsies of rheumatic heart disease decided that there was no conclusive evidence that pregnancy shortens the life of the patient suffering from rheumatic heart disease. Daly and Strouse feel that there is no appreciable difference at the end of several years between those cardiacs who have gone through a pregnancy and those who have not. However, the fact that a certain heart has stood one pregnancy well is no proof that it will stand the strain of another pregnancy. Our own few cases that came back seem to indicate quite the contrary, although we must be careful in drawing conclusions from such a small group.

#### CONCLUSIONS

1. The cardiac pregnant woman will get better care as a result of the combined efforts of the cardiologist and the obstetrician.

2. In determining whether a given heart will stand the strain of pregnancy, labor, and delivery, more attention should be paid to the cardiac reserve and less to the valvular lesion.

3. Contrary to the general impression that cardiac patients have short labors, eighty-two of our primiparas had an average labor of 20.5 hours.

4. The management during pregnancy of the cardiac who is allowed to continue her pregnancy must constantly aim either to maintain or build up her cardiac reserve. This is best accomplished by proper balancing of rest and work.

5. During labor the pregnant cardiac patient should be given sufficient rest and analgesia with morphine and scopolamine or with one of the barbiturates.

6. The pulse and respirations are the best guides as to the behavior of the heart during labor.

7. The second stage with its severe strain on the myocardium should be shortened as frequently as possible, especially if there is an increase in pulse and respirations.

8. If labor threatens to be prolonged, if progressive toxemia is present, or if there is any degree of disproportion, the case is best handled by cesarean section under local infiltration.

9. The pregnant cardiac patient who has had a break in compensation should be hospitalized and treated, and after the heart has become well compensated, the pregnancy should be terminated by cesarean section and sterilization under local anesthesia. This procedure should also be done for patients with a severe aortic lesion and those showing definite evidence of myocardial damage.

10. While there is no conclusive evidence that pregnancy shortens the life of the cardiac patient, yet the fact that one pregnancy does no harm is no proof that another pregnancy will do no harm. In fact, some of our patients who came back to be delivered again showed the reverse to be true.

#### REFERENCES

- (1) *Stander, H. J., Duncan, E. E., and Sisson, W. E.*: AM. J. OBST. & GYNEC. 11: 44, 1926. (2) *Hamilton, B. E., and Kellogg, F. S.*: Ibid. 13: 535, 1927. (3) *Gorwin, J., Herrick, W. N., Valentine, M., and Wilson, J. M.*: Ibid. 13: 617, 1927. (4) *Pardee, H. E. B.*: Ibid. 17: 255, 1929. (5) *Reid, W. D.*: Ibid. 19: 63, 1930. (6) *Daly, P. A., and Strouse, S.*: J. A. M. A. 96: 1655, 1931. (7) *Stander, H. J., and Cadden, J. F.*: AM. J. OBST. & GYNEC. 24: 13, 1932. (8) *Scott, W. A., and Henderson, D. N.*: Ibid. 27: 342, 1934.

1325 UNION STREET

---

Guyot, J., Courriades, H., and Rocher, C.: Metrorrhagia in the Menopause, Bull. Soc. d'obst. et de gynéc. 23: 717, 1934.

Recent statistics have shown that 60 per cent of the cases of metrorrhagia during the menopause require no surgical treatment because the etiology is a benign modification of the uterine mucosa. The authors collected twenty-five cases of metrorrhagia among women in the change of life and found cancer of the body of the uterus in 18 per cent, cancer of the cervix in 9 per cent, fibroids in 18 per cent, polyps in 14 per cent, and hyperplasia in 50 per cent. These authors maintain that exploratory curettement permits a more definite diagnosis than hysteregraphy with lipiodol or intrauterine exploration with a hysteroscope. The authors have never seen a curettement fail to discover the lesion. Dissemination of carcinomatous cells with curettement is extremely rare.

J. P. GREENHILL



# THE INJECTION OF VARICOSE VEINS DURING PREGNANCY\*

## A PRELIMINARY REPORT

GOODE R. CHEATHAM, M.D., AND ABEL E. PECK, M.D., ENDICOTT, N. Y.  
(From the Obstetrical Department of Endicott-Johnson Medical Service and Ideal Hospital)

THE injection method of treatment of varicose veins dates back to the invention of the hypodermic syringe in 1851. Pravas and Chasaignae (1853) injected ferrie chloride to coagulate the blood. Deranges in 1855 advocated iodotannic solution. These, together with many other solutions, were tried and found to be so irritating that they were abandoned. Chiefly due to Linser, 1911, and Secord and Nabl, sodium salicylate and glucose were tried and found to give good results. Since 1921 many thousands of cases have been reported with good results with glucose, dextrose, quinine urethan, sodium chloride, sodium salicylate, and sodium morrhuate.

Of the many thousands of cases reported the most common type of varicose veins, namely that of pregnancy, was conspicuous by its absence, or it was stated empirically that pregnancy was a contraindication. This attitude is further reflected by DeLee<sup>1</sup> when he states the dangers of varicosities of pregnancy as ulceration, phlebitis, emboli, and rupture with fatal hemorrhage, then adds under treatment, "Little can be done to cure the bad cases of varicosities during pregnancy, but I have helped several cases by the administration of calcium." Much the same attitude is expressed by Williams<sup>2</sup> who states, "Active treatment is useless in vulval varices, but the danger of their rupture at the time of labor should be borne in mind."

De Takats<sup>3</sup> states, "Venous pressure in the lower extremities rises with the advance of pregnancy. Existing varicose veins are aggravated. They do not recede after childbirth, but get progressively worse with each pregnancy. The question arises whether it is advisable to treat the veins during pregnancy or whether it is better to wait until after childbirth. Based on a small experience with pregnant women (six cases), we found that the injection treatment gave them subjective relief, and if the main saphenous trunk was obliterated or ligated, the progress of the disease could be stopped. This, of course, is true only of the true varicose veins. If the deep circulation is obstructed, and if the coexisting lymphatic block produced edema, the injection treatment is obviously not indicated and will not influence a postpartum phlegmasia. This important field, pregnancy and varicose veins, needs further investigation and study."

\*Presented at Clinical Conference, Charles S. Wilson Memorial Hospital, Johnson City, N. Y., April 4, 1935.

Hawk<sup>4</sup> states, "Pregnancy when complicated by varicose veins is a decided indication for injection. Great relief is afforded these women and the procedure may be carried out up to the sixth or seventh month safely. Quinine solutions should not be used."

McPheeters<sup>5</sup> published a report based on the treatment of varicose veins in 46 otherwise normal pregnancies with the following conclusions:

1. "Often a pregnant woman is made an invalid by the pain and disability occasioned by the occurrence of varicose veins and their complications.

2. "In the past, the treatment has been only symptomatic and temporary.

3. "We should no longer accept the opinion of many men that women must have pain and discomfort during pregnancy unless the causative factors cannot be removed.

4. "Injection of varicose veins during pregnancy lessens the tendency to thrombophlebitis after delivery, since the blood is more or less stagnant in a varix.

5. "It is perfectly safe to inject varicose veins during pregnancy, and by so doing we can relieve the woman of her pain and discomfort in the course of one or two weeks."

Kilbourne<sup>6</sup> in a discussion of varicose veins of pregnancy gives no personal experience with the injection of varices during pregnancy, but in commenting on McPheeters' report states, "If a pregnant patient is in serious pain or discomfort, I see no objection to allowing relief by the simple expedient of injecting veins; as to the question of preventing milk leg by previous varicose vein injection, I know by clinical experience that varicose veins do develop phlebitis with a frequency not found in normal veins, however, phlegmasia alba dolens most often begins in the deep veins of the legs and later involves the superficial veins. General treatment of varicose veins of pregnancy as a prophylactic against phlebitis would not be advised. In the majority of light cases it is preferable to wait until after delivery and see if the varicose veins will not retrogress spontaneously; however, the treatment is indicated in patients with serious distress during the fourth to the seventh month of pregnancy."

These few concessions that varicose veins of pregnancy can be injected mark a fundamental change. If we study the history of any medical or surgical advancement, we find that the pregnant woman is the last to receive its benefits. For years no one dared do an appendectomy on a pregnant woman. More recently the same was true of thyroidectomy, yet no one now hesitates when these procedures are indicated. The objections to treating varicose veins of pregnancy are long standing and deeply ingrained into the public and the profession. Ambrose Pare<sup>7</sup> wrote of them in 1579. "Women with child are commonly troubled with them by reason of the heaping together of their suppressed menstrual evacuation. It is best not to meddle with such as are inveterate for such being cured there is to be feared a reflux of the melancholy blood to the noble parts whence there may be danger of malign ulcer, a cancer, madness or suffocation." Pigeaux warned of a case of abortion in a cook following the bandaging of varicose veins. The same deep-seated objections to treatment during pregnancy are seen today when week after week we see in the office patients with large painful varicose veins who refuse treatment be-

cause of their own fear of being treated until after delivery, or because they have previously and usually repeatedly been told by physicians that they should wait until after delivery for treatment. Further evidence of this opposition to treatment is seen in the fact that we were able to treat only twenty-four patients during the past nineteen months, while we had 503 deliveries during that time. This is rather more impressive when we consider that DeLee<sup>8</sup> states, "Nearly everyone has at least one or more phlebeetasiae. In 20 per cent of the cases the varicosities are marked."

It should be mentioned here in partial explanation of the small percentage of treated cases that in no case was injection treatment urged upon any patient. We wanted an honest opinion from the patient as to the benefit, if any, she derived from the treatment, and we did not feel that we would get an unbiased opinion if the patient already had a definite fear or opposition to treatment during pregnancy, and especially if her objections were founded on advice from her family physician. It was chiefly because of this combined opposition of patients and doctors that it was decided to give this preliminary report much earlier than was originally intended.

The purpose of this work was twofold:

1. To prove the injections of varicose veins of pregnancy a safe procedure at any stage of pregnancy, for any size varix at any location.
2. To try and arrive at some definite conclusion as to which veins should be injected and which left alone.

To do this we have injected every case of varicose veins of pregnancy which would submit to treatment. We have set no limitations on the location or size of the varix. We have set no limitations on the period of the pregnancy, except that no injections were done in the last two weeks of pregnancy, and this limitation was set because we wanted all patients ambulatory during treatment. The contraindications for varicose veins of nonpregnant patients have been observed. Sodium morrhuate was used exclusively. We submit twenty-four cases. Of these, twenty-two are delivered. The site of injection ranges from the ankle to Poupert's ligament and the vulva. The size of the veins treated varies from superficial, unimportant varices (three cases) to varicose veins so extensive as to force the patient to be in bed. One patient came to the office via ambulance until after injections were started. The number of injections varied from one to seven. The average injection was 3 c c. The ages of the patients varied from eighteen to thirty-seven years. The earliest stage of pregnancy when treatment began was four months, the latest seven and one-half months. Several were treated to within fourteen days of expected delivery. There were three primiparas in the series.

## RESULTS

We had one local reaction with no untoward results for mother or baby. No treated patient failed to be relieved. No treated patient had any postpartum complication with the circulatory system. No treated patient was hospitalized longer than the untreated patient. Each patient on completion of the treatment was asked this question, "If, now that you have had the treatment and know what it is like, you had the choice of keeping the veins or having the treatment, which would you choose?" Two chose the veins, the remainder the treatment.

## REFERENCES

- (1) *DeLee, Joseph B.*: Principles and Practice of Obstetrics, ed. 5, Philadelphia, W. B. Saunders Co., Chapter IV, pp. 108, 109, 1929. (2) *Williams, J. Whitridge*: Obstetrics, ed. 6, New York, 1930, D. Appleton Co., Chapter XXIV, p. 598. (3) *De Takats, Geza, and Quint, Harold*: Surg. Gynec. Obst. 50: 545, 1930. (4) *Hawk, George W.*: Pennsylvania M. J. 34: 859, 1931. (5) *Mc Pheters, H. O.*: Lancet 51: 589, 1931. (6) *Kilbourne, Norman J.*: AM. J. OBST. & GYNEC. 25: 104, 1933. (7) Johnson's Translation 1634. Maladies des Vaisseaux 1843 from Kilbourne as above. (8) *DeLee, Joseph B.*: Principles and Practice of Obstetrics, ed. 5, Philadelphia, 1929, W. B. Saunders Co., Chapter XXIX, p. 412.

208 JEFFERSON AVENUE

## MOTILITY IN THE TRANSPLANTED, DENERVATED UTERUS\*

SANFORD KAMINESTER,† M.D., AND SAMUEL R. M. REYNOLDS, M.A., PH.D.,  
BROOKLYN, N. Y.

(From the Department of Physiology of the Long Island College of Medicine)

THE purpose of the present investigation is to demonstrate the relationship between the innervation (extrinsic and intrinsic) of the rabbit's uterus and the myometrial action of estrin and progestin. Ample evidence exists to show that estrin is specifically necessary for initiation of coordinated rhythmic motility and for the sustaining of such activity in the normal uterus.<sup>1-6</sup> It is also known that progestin, on the other hand, exerts a very strong inhibiting effect on rhythmic, estral contractions.<sup>6-12</sup> That portions or all of the excised uterus will contract rhythmically and under suitable circumstances even simulate parturition has, of course, long been known. It has only recently been shown, however, that spontaneous rhythmic motility is observed in vitro only when the uterus is under the influence of estrin at the time it is removed from the body.<sup>3, 4</sup> The fact that the excised, quiescent uterus cannot be made to contract rhythmically by treatment with estrin even though large quantities be added to the perfusion bath is most important.

The present experiments have been done to ascertain the effects of estrin and progestin on the transplanted denervated uterus.

\*Added by a grant from the Committee for Problems in Research of Sex, of the National Research Council.

†Member of Department of Obstetrics and Gynecology.

## EXPERIMENTAL

The plan of the experiments was a simple one. One uterine horn was transplanted, as described below, from its normal site to a position on the anterior abdominal wall, there taking up a new blood supply. In the process of completing this transposition, all the original nerves to the uterus were severed. Inasmuch as sufficient time was allowed for complete degeneration of the nerve paths and since it has been shown that there is no extensive intrinsic uterine motor nerve plexus,<sup>16</sup> it was possible for us to investigate in the essentially denervated uterus two things: first, the degree of activity associated with various sexual states, viz., oophorectomy, estrus, and pseudopregnancy; and second, the effect of replacement therapy with estrin.

## STEPS IN THE OPERATION

*First Stage (Fig. 1).*—A mature female rabbit, weighing approximately  $3\frac{1}{2}$  kg. was anesthetized with ether. A longitudinal incision was made to the right of the

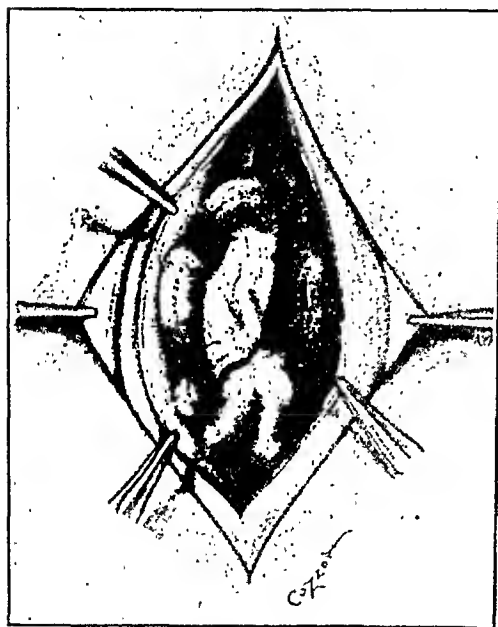


Fig. 1.—Operation, first stage.

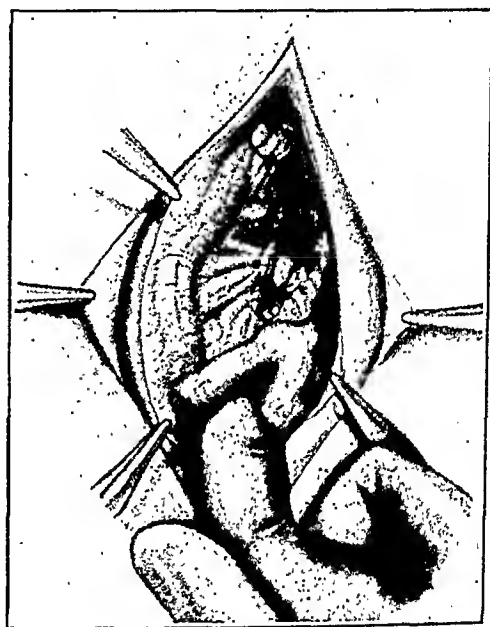


Fig. 2.—Operation, second stage.

midline, starting about three centimeters above the symphysis and extending cephalad a distance of six to eight centimeters. The right uterine cornu was brought up into the wound, the tubal end clamped, transected, and ligated, the ligature including the ovarian artery and whatever veins accompany it. The free border of the uterus was then scarified as was an area on the peritoneal surface of the anterior abdominal wall parallel to the original incision and about a half centimeter lateral to it. The scarified areas were approximated by means of interrupted sutures of plain catgut. These sutures penetrated half the thickness of the muscle coat of the uterus. At the conclusion of this stage there was a ventrofixation of the uterus.

*Second Stage (Fig. 2).*—After an interval of from one to three weeks or even longer, the second stage was undertaken. The abdomen was again opened, this time in the midline in order to avoid adhesions. The index finger of the left hand was passed over the cervical region of the uterus into the channel produced by the adhesion of this organ to the anterior abdominal wall. In this way the entire mesometrium was brought into view. This tissue was then incised and ligated with

interrupted catgut suture ligatures in such a manner as to sever the uterus from its normal surroundings except for its cervical attachment.

*Third Stage (Fig. 3).*—After another interval of from one to three weeks, the animal was opened for the third time. The vaginal tube was transected, care being taken to include all remaining mesometrial tissue on the right side. The left uterine cornu was then severed close to the cervix. As a result, the transplanted uterus terminated in a cuff of vagina containing two cervices. The entire organ was dependent for its nutrition on the vessels passing through the adhesions along the abdominal wall and also occasionally those to the intestines. The vaginal cuff was brought up through the incision and anchored to the skin so that the two cervices protruded. Records of motility were obtained by the method described by one of us,<sup>9</sup> using pressure changes in a balloon inserted through the fistula.

In some animals at the beginning of the third stage, the transplanted uterus was

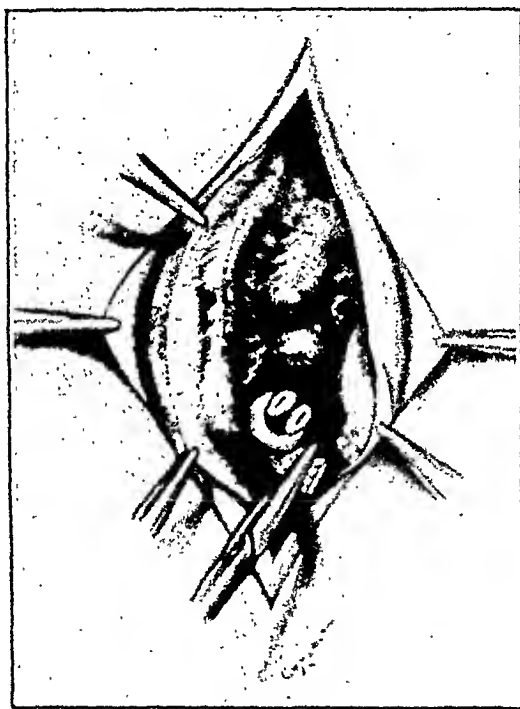


Fig. 3.—Operation, third stage.

severed from its cervix, leaving intact the vaginal canal, the two cervices, and the normal left uterus. The lowermost portion of the right uterine cornu was brought up through the abdominal wall, resulting in a transplanted, cervicectomized uterus. In addition, a fistula was sometimes made using the nontransplanted left uterus according to the method previously described.<sup>5</sup> Contractions were then recorded in the same fashion as in the noncervicectomized uterus.

The above operative procedures have been previously described<sup>10</sup> but are included for the sake of completeness.

#### RESULTS

The following results are based upon data obtained from seven rabbits. In order to determine whether the nerve paths had been entirely severed, the presacral nerve was stimulated in each animal just before it was killed. Data from those rabbits in which a response of the uterine transplant was elicited were rejected. Although the number of rabbits finally

used is admittedly few, the completeness of the operation and the consistency of the results give ample evidence of the activity of the denervated uterus in response to stimulation by the ovarian hormones, estrin and progestin.

The results are presented under two headings, relating to the activity of each of the hormones mentioned.

1. Rhythmic contractions of the transplanted uterus. We observed rhythmic motility under three distinct circumstances:

A. Very marked contractions occurred spontaneously in two rabbits in which the ovaries were left in situ. Such motility is present in the nontransplanted uteri when nonpregnant rabbits are in heat and is lacking when they are not in heat.<sup>2</sup> Large graafian follicles normally present when this estral motility is observed were present in these animals. Thus, it is demonstrated that the transplanted uterus is capable of exhibiting normal estral motility. The hormone specifically responsible for such motility is known to be estrin.<sup>2</sup>

B. In three animals, ovariectomy was performed and then estrin (theelin\*) was injected. In one of these in which the cervix had been severed, the effect was observed twice. Four times, therefore, it was found that estrin induced rhythmic motility in a previously quiescent, transplanted uterus (Fig. 4).

C. In another rabbit, rhythmic motility followed an extended interval of inactivity during a period of pseudopregnancy (Fig. 6).

Thus it is clear that not only can rhythmic contractions be sustained in a transplanted uterus, but they can be initiated as well. Moreover, this is true whether or not the cervix is attached to the transplanted tissue.

2. Hormonal inhibition of motility in the transplanted uterus. In three animals made pseudopregnant by the injection of pregnancy urine, spontaneous motility was inhibited. It was found that at this time we were unable to induce motility (Fig. 5, A) by means of estrin. Thus, the transplant was found to be unresponsive to its normal hormonal excitant, estrin, when under the influence of progestin, furnished by the rabbit's own corpora lutea.

These results are consistent in every way with earlier observations<sup>8, 10</sup> which showed that, when the nontransplanted uterus is under the influence of progestin, it is quiescent and cannot respond with rhythmic motility to estrin administration.

#### PROTOCOLS

*Protocol 1.*—Animal 573 (Fig. 4).

Nov. 17, 1934: First operative stage.

Jan. 26, 1935: Second operative stage.

Feb. 7, 1935: Third stage and ovariectomy, bilateral. Fistula of cervicectomized right uterus, transplant.

Feb. 10, 1935: Record (Fig. 4, A). No spontaneous motility in normal uterus; no record made from transplant.

\*Generously furnished by Parke, Davis and Co.

- Feb. 11, 1935: Theelin, 100 rat units, intravenously.
- Feb. 12, 1935: Record (Fig. 4, *B*). Normal fistula showed moderate motility but some degree of irregularity. Cervicectomized transplant showed very slight motility. Theelin 100 rat units.
- Feb. 13, 1935: Record (Fig. 4, *C*). Normal fistula, good motility, fair regularity. Transplant, good motility and fair regularity. Theelin 100 rat units.
- Feb. 14, 1935: Record (Fig. 4, *D*). Normal fistula showed good motility and more regular contractions than Feb. 13, 1935. Transplanted fistula also showed better motility and regularity. Theelin 100 rat units.

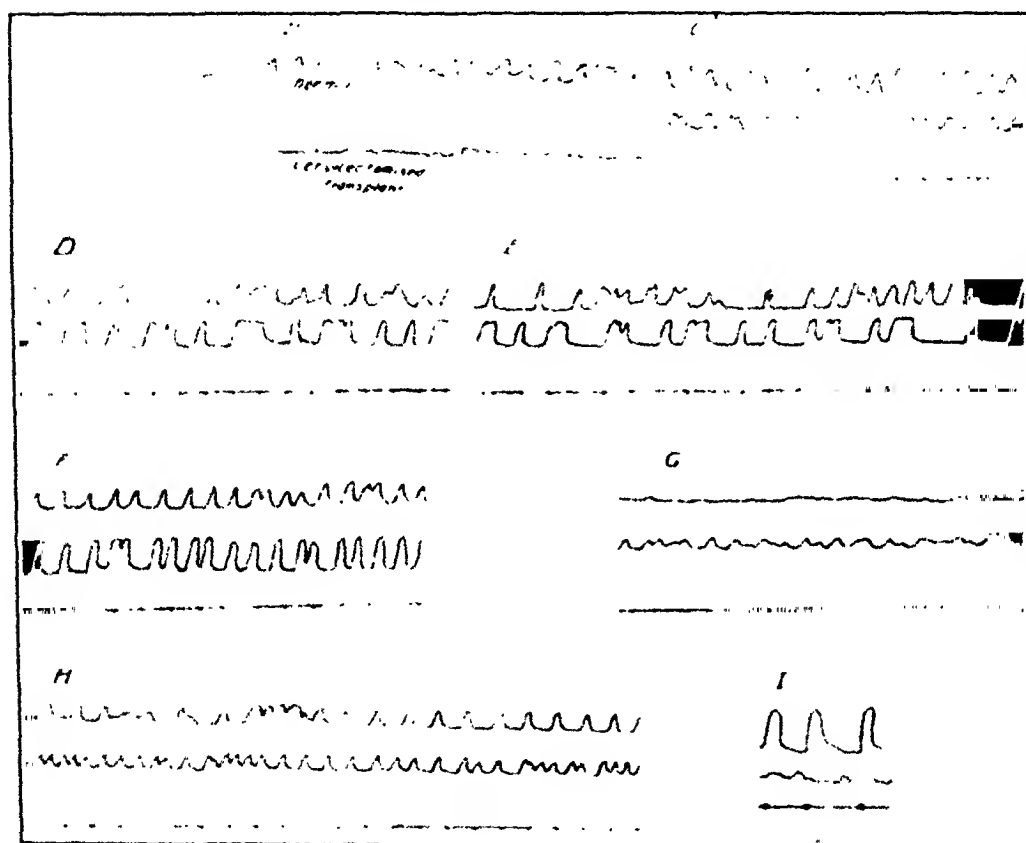


FIG. 4.—For explanation, see Protocol 1, animal 573, and text.

- Feb. 15, 1935: Record (Fig. 4, *E*). About the same as Feb. 14, 1935.
- Feb. 16, 1935: Record (Fig. 4, *F*). Rhythmicity very definite, contractions strong.
- Feb. 18, 1935: Record (Fig. 4, *G*). No theelin for four days. Normal fistula showed no contractions, transplanted fistula a few irregular small contractions. Theelin 50 rat units.
- Feb. 19, 1935: Theelin 50 rat units.
- Feb. 20, 1935: Record (Fig. 4, *H*). Contractions returning, normal uterus somewhat irregular, transplant more nearly regular.
- Record (Fig. 4, *I*). Animal anesthetized with dial, abdomen opened. Transplant in excellent condition, no infection. Pre-aclral nerve stimulated. Response in normal, not in transplanted uterus.



*Protocol 2.—Animal K-15 (Fig. 5).*

- Jan. 3, 1935: First stage, right ovariectomy.  
 Jan. 17, 1935: Second stage.  
 Feb. 4, 1935: Third stage.  
 Feb. 6, 1935: Five cubic centimeters of urine of pregnancy.  
 Feb. 11, 1935: Theelin, 150 rat units.  
 Feb. 12, 1935: Record (Fig. 5, *A*). One week pseudopregnant. No motility in either the normal or transplanted fistula. Operation—left ovariectomy. Many large corpora lutea seen.  
 Feb. 13, 1935: Theelin, 75 rat units.  
 Feb. 14, 1935: Record (Fig. 5, *B*). Marked motility in both the transplanted and the normal fistulas.

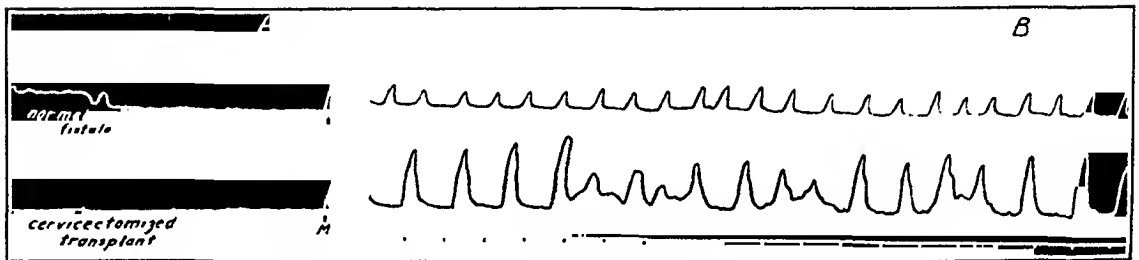


Fig. 5.—For explanation, see Protocol 2, animal K15.

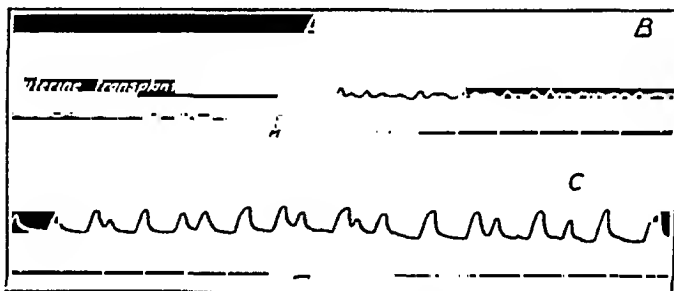


Fig. 6.—For explanation, see Protocol 3, animal K2.

*Protocol 3.—Animal K-2 (Fig. 6).*

- Sept. 8, 1934: First stage.  
 Sept. 22, 1934: Second stage.  
 Oct. 3, 1934: Urine of pregnancy, 10 c.c.  
 Oct. 5, 1934: Third stage. Some sloughing of the cervix, the rest of good color. Very easy access with balloon.  
 Oct. 16, 1934: Record (Fig. 6, *A*). Thirteenth day of pseudopregnancy. No motility in the transplant.  
 Oct. 17, 1934: Theelin, 50 rat units.  
 Oct. 18, 1934: Theelin, 150 rat units.  
 Oct. 19, 1934: Record (Fig. 6, *B*). Sixteenth day of pseudopregnancy. Slight motility, irregular. Theelin, 50 rat units.  
 Oct. 22, 1934: Record (Fig. 6, *C*). Nineteenth day of pseudopregnancy. Large contractions, rhythmic motility in transplant.

## DISCUSSION

There exists in the literature ample evidence to show that uterine function is not materially modified when the nervous connections of that organ to the central nervous system are severed. Those who have transected the spinal cord,<sup>17</sup> destroyed it<sup>17</sup> or performed lumbar sympathectomy without subsequent interruption of conception, gestation, and parturition,<sup>18</sup> justifiably claim that such nervous connections are probably not essential for the functioning of the uterus. Our results confirm this conclusion, as regards the estral and pseudopregnant uterus. It is a fact, however, that those who have heretofore claimed to have severed the main nerve paths to the uterus have also failed to adduce undeniable proof of the completeness of their operations. We have taken this precaution and have accepted as satisfactory only those animals in which the transplant failed to respond when the presacral nerve was stimu-

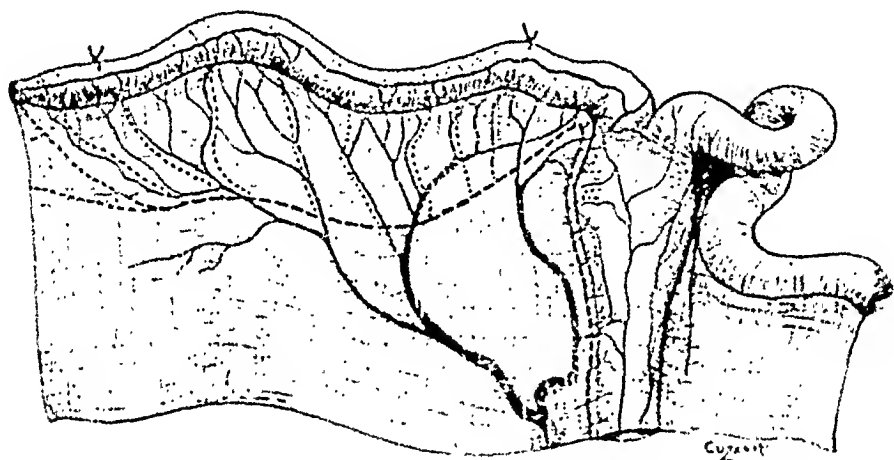


FIG. 7.—Innervation to uterus, shown in broken lines. (Reprinted from *Am. J. Physiol.* 112: 616, 1935.)

lated. The results of the present study show unmistakably, therefore, that the connection of the uterus to the central nervous system is not essential for the known action of estrin and progesterin. Yet, one may ask, to what extent do these hormones depend upon the intrinsic innervation of the uterus for their effects?

The main peripheral paths of the motor sympathetic innervation of the rabbit uterus lie in the parametrium and are distributed to each cornu locally, forming no extensive intrauterine connections<sup>19</sup> (Fig. 7). It is also true that the cervical ganglia play no essential part in regulating the responses to the hormones studied since the cervix has been removed in some of the transplants without modification of the activity. Because, then, the uterus without the cervix is virtually devoid of nerve cells and because in the procedure of transplanting the uterus all the parametrium is severed and ample time allowed for degeneration, we are forced to the conclusion that the stimulating action of estrin on the

one hand and the inhibiting effect of progestin on the other are each mediated independently of the extrinsic and intrinsic motor sympathetic innervation.

It should be noted in passing that Langley and Anderson have shown that there are no inhibitory sympathetic fibers to the rabbit uterus and that there is no sacral autonomic innervation. While this last has been questioned, certainly the sacral autonomic innervation to the uterus is at best inappreciable.

In view of the above considerations it would appear, therefore, that the ultimate rôle of estrin and progestin activity in relation to uterine musculature must be investigated through the chemical changes that take place in the uterus itself following the administration of these hormones. But the possibility that the synergistic action of other endocrine factors may be essential for the normal effect of these hormones must not be overlooked.

#### CONCLUSIONS

1. Estrin maintains rhythmic contractions in the transplanted uterus.
2. Estrin also induces such contractions in the previously nonmotile transplanted uterus.
3. Progestin inhibits estral rhythmic contractions in the transplanted rabbit uterus.
4. The myometrial effects of these two hormones are essentially myogenic, the extrinsic and intrinsic innervation being nonessential.
5. Although the action of estrin is myogenic, this hormone is incapable of inducing rhythmic contractions *in vitro* but can do so in the transplanted uterus *in vivo*.

#### REFERENCES

- (1) Frank, R. T., Bonham, C., and Gustavson, R.: *Am. J. Physiol.* 74: 395, 1925. (2) Reynolds, S. R. M., *Am. J. Physiol.* 97: 706, 1931. (3) Blair-Bell, W., Datnow, M., and Jeffcoate, T.: *J. Obst. & Gynaec. Brit. Emp.* 40: 541, 1933. (4) Newton, W. H.: *J. Physiol.* 79: 301, 1933. (5) Robson, J. M.: *Recent Advances in the Physiology of Sex and Reproduction*, Philadelphia, 1934, P. Blakiston's Son & Co. (Churchill). (6) Morgan, T. N.: *J. Obst. & Gynaec. Brit. Emp.* 40: 1196, 1933. (7) Knaus, H.: *Klin. Wchnschr.* 9: 839, 1930. (8) Reynolds, S. R. M., and Friedman, M. H.: *Am. J. Physiol.* 94: 696 and 705, 1930. (9) Reynolds, S. R. M.: *Am. J. Physiol.* 98: 230, 1931. (10) Reynolds, S. R. M., and Allen, W. M.: *Am. J. Physiol.* 102: 39, 1932. (11) Robson, J. M.: *Quart. J. Exper. Physiol.* 22: 209, 1932. (12) Tausk, M., de Fremery, P., and Luchs, A.: *Acta. brev. med.* 1: 4, 1931. (13) Fevold, H., and Hisaw, F. L.: *Proc. Soc. Exper. Biol. & Med.* 39: 620, 1932. (14) Blair-Bell, W., Datnow, M., and Jeffcoate, T.: *Ibid.* (15) Allen, W. M., and Reynolds, S. R. M.: *AM. J. OBST. & GYNEC.* 30: 309, 1935. (16) Reynolds, S. R. M., and Kaminester, S.: *Proc. Soc. Exper. Biol. & Med.* 32: 1149, 1935. (17) Marshall, F. H. A.: *Physiology of Reproduction*, New York, 1922, Longmans, Green & Co., p. 570. (18) Bach, Z. M., *et al.*: *Am. J. Physiol.* 99: 444, 1932. (19) Kaminester, S.: *Proc. Soc. Exper. Biol. & Med.* 32: 1147, 1935.

## ELECTROUTEROGRAPHY

HENRY C. FALK, M.D., AND RALPH NAHON, M.D., NEW YORK, N. Y.

(From the Gynecological Service and the Cardiological Department of the French Hospital)

THE following means have been employed to study and report the contractibility of the uterus:

1. Abdominovaginal palpation of the human uterus
2. The muscle strip method in animals
3. Observation of exposed or excised animal uteruses
4. Mechanical tracings of pressure variations
5. Uterosulpingography
6. Electrical methods

1. *Palpation of the Human Uterus.*—Much information on the form variations, contractions, etc., of the human uterus can be obtained from the simple procedure of bimanual palpation in trained hands.

Dickinson (*Human Sex Anatomy*) presents a thorough survey of the information to be gained from such an examination. Furrows and ridges, areas of hardenings and softenings, changes in shape, size, and position, all give evidence of the activity of the nonpregnant uterus. He says, "The uterus appears to me to develop special degrees and rhythms of contraction at the time of ovulation, . . . relative quiescence follows menstruation, then activity develops during the time both ovaries are large and tender and while one shows protrusion, and then distinctive quiescence recurs until just before menstruation."

2. *The Muscle Strip Method.*—A strip of uterine muscle is so arranged that its contractions are recorded on a kymograph by a muscle lever, giving a mechanical tracing.

With this method Blair (1922), using the white rat, showed the maximum contractions to be greater during diestrus than during estrus. Keyes (1923) using excised muscle strips of the domestic sow, demonstrated the differences in the spontaneous rate of contraction at different times in the estrus cycle. He demonstrated two types of contractions, large and small, occurring at the same time. During the period of development of the graafian follicle and shortly after its rupture, the large contractions predominate. Keyes believes that the maturing corpus luteum inhibits the large contractions and causes the short contractions to predominate.

3. *Observations on the Excised or Exposed Animal Uterus.*—The excised whole uterus when kept at body temperature in oxygenated Locke's solution may be restored to spontaneous contraction.

Seckinger (1923) studied the contractions of the tube of the sow in vitro. He states that contractions appear first about nineteen days before rupture and terminate

after the follicles have ruptured and the ova have entered the uterus. During the ripening of the follicle the contractions are short and rapid. After the ova appear in the uterus, the contractions change to a slow rhythm. Wislocki and Guttmacher (1924), studying the uterus and tubes of the sow, verified the cyclic changes observed by Seckinger. Brouha and Simmonet (1927), using the guinea pig's uterus, made periodic observations on a series of excised contracting uteri and confirmed the differences in rate and strength of contractions at different points in the estrous cycle.

Ingenuous methods were devised for observing the uterus in situ in the living animal. Wijsenbeek (1922), Mikulicz-Radecki and Westman (1926) so attached the cecum to the abdominal wall in rabbits as to wall off the uterus from the other abdominal organs, and then installed a small glass window in the abdominal wall so that the uterus and tubes could be observed. Mikulicz-Radecki found the abdominal window method unsatisfactory and reverted to the muscle strip technic. Westman (1926) working on rabbits found very active muscular contractions of the tube in connection with follicular ripening. These contractions were strongest during estrus just before rupture when ripe follicles are present. He believes the corpus luteum has an inhibiting effect on the contractions.

4. *Mechanical Tracings of Pressure Variations.*—While the uterus is contracting, the cavity naturally undergoes variations in size. If the cavity be filled with fluid, this fluid undergoes variations in pressure. If a tube is led from this fluid to a manometer or a tambour and a lever installed, a kymographic record of these pressure changes can be made which will be a fair index of uterine contractility under conditions involving an irritant within the cavity.

The fluid in the cavity of the uterus may be lying free, in which case a cannula is introduced into the cervix to make an air-tight system. On the other hand, this fluid may be contained in a rubber bag or balloon which is introduced into the uterine cavity first and later is distended with fluid.

Two interesting early experiments of this sort are mentioned in Dickinson's *Human Sex Anatomy*. Heinricus (1889) and Aceonci (1891) introduced small rubber balloons into the uterine cavity by means of narrow silver sounds. The balloons were filled with water and the water column connected to recording manometers.

Heinricus notes three sorts of contractions: those synchronous with the pulse which he considers pulsation of a uterine artery and which are inconstant depending on impingement on or near such an artery, those which are respiratory in rhythm which also vary in clearness, and finally, those which seem clearly uterine. He gives the duration of a contraction as varying from thirty seconds to three minutes.

Aceonci also notes the presence of uterine contractions in the nonpregnant human uterus but gives the rate of contraction as seven to eight per minute.

Reynolds (1929) introduced into rabbits' uteri a tiny rubber balloon which he filled with water. This was preceded by an operation, hemisecting the vagina and creating a uterovaginal-abdominal wall fistula which gave better access to the uterus. Excellent kymographic tracings were obtained but the question arises, as in all these methods, whether artificial distention of the uterus effects or distorts contractions and gives a picture or rhythm unlike those that are spontaneous. He made no attempt to draw any exact conclusions.

Knaus (1929) used this method in extensive studies on ambulatory patients. He filled the uterine cavity with oil and depended on the conic shoulder of the salpingography cannula to keep the system air tight. The result of these studies, which depended upon the principle that pituitrin is ineffectual in causing uterine contractions in the presence of a corpus luteum, was roughly to fix the date of ovulation with special reference to the "safe period." He found normal uteri in women with twenty-eight-day cycles; spontaneous rhythmical contractions occur during the first fourteen days of the cycle and the uterus at this time responds to injections of pituitrin. Beginning at the sixteenth day, there are no more spontaneous rhythmical contractions and no response to pituitrin. The return of uterine activity does not occur until the day preceding menstruation.

Very recently Adair and Davis (1933) introduced rubber bags into the post-partum human uterus. The bags were distended with sterile water. The kymographic tracings were very clear. The effects of certain oxytocic drugs were shown.

5. *Uterosalpingography*.—A natural outcome of the x-ray picture of the uterine cavity filled with an opaque medium was the "G. I. Series" of the uterus, and the observation, under the fluoroscope, of the continuous variations in size and shape of the outline of the distended or partly distended uterine cavity.

Schultze (1929) made this the means of extensive studies of the mode of contraction of the uterus in ambulatory cases. These studies seem to show that the uterus has three functionally contracting segments, the main part of the fundus and the two horns. Both maximal contractions involving all three segments and partial contractions involving only one or two segments occur or progress from above downward. In this work the contraction of the uterus seems to have as its partial object, the emptying of the uterus of its unnatural contents. Therefore the objection arises that while the manner of contraction may be characteristic, the stimulus to contraction may be of artificial provocation.

6. *Electrical Methods*.—These are based on the familiar "action-current" of contracting muscle. As in the case of the electrocardiograph, two contacts are required to "lead off." The type of contact point varies. Some observers have used metal electrodes (usually silver), others have used physiologic or nonpolarizable electrodes. Leads have been taken in animals from points on the external surface of the exposed tube and uterus; in human beings, from the cervix, the rectum, the external abdominal wall, and even the extremities. The recording instrument has usually been some form of string galvanometer.

Work of this nature was begun about 1910. Theilhaber (1910) placed one electrode on the cervix and the other in the rectum at the height of the fundus. He obtained curves by this method which apparently were not cardiac or respiratory. They were not present in women after the menopause or in cases following hysterectomy. However, since they were not followed through the entire cycle from one period to the next, we have no way of correlating them with the behavior of the uterus at various parts of the cycle.

Veit (1912) attempted to record the uterine contraction coincident with labor pains, apparently with little success. He obtained records of contractions when he

used a lead from the feet, but when the arms were used the heart contractions obliterated all others. Blumenfeldt and Dahlman (1913) obtained records by leading directly from the puerperal uterus of laparotomized rabbits. The uterus, in this work, was abnormally stimulated. A pressure system recorded mechanical curves at the same time, and it was noticed that the electrical and mechanical oscillations were not simultaneous. Metal electrodes were used.

Greene (1928) working with nonpolarizable electrodes on the excised automatically contracting rat uterus noticed two different electrical curves, a slow, large deflection of thirty- to forty-seconds' duration and small, rapid deflections of about one hundred and twenty per minute. Myograms were taken at the same time and the electrical action currents were found to start before the mechanical contractions.

Bode (1931) obtained electrometrograms of the pregnant human uterus which he stimulated to contraction with injections of pituitary gland secretion.

A very thorough piece of work was done on the exposed uterus of the virgin rabbit in situ by Bun-ichi Hasama (1930), using nonpolarizable electrodes. Needle electrodes were also tried and gave similar results. He was able to show the registration of the action current of observed peristaltic muscle waves that passed through the uterus, from tubal cornu to cervix. The electrometrogram was a regular diphasic curve with the approximate rate of three to seven curves per minute. The intensity of the action current curves and the mechanical movements were not always parallel. The frequency and amplitude of the electrical curves varied in different parts of the uterus. Action currents could be obtained from the circular musculature, the amplitude of which was less but the frequency the same as the longitudinal.

A still more recent piece of work along this line was that of Vozza (1933) who ran an electrical and a mechanical pressure system in parallel. Both systems were so arranged as to register on the same strip of film. The pressure system was "led off" from the uterine cavity through a small opening in one of the uterine cornua. The electrodes were of silver and were placed upon the ends of the isolated cornu. The rabbits in this experiment were at the beginning of pregnancy.

Vozza concludes that "there was a rather intimate relation between the mechanical contractions and the bioelectrical phenomena, but the bioelectrical changes preceded by a fraction of a second the mechanical movements." There were, however, occasional exceptions to this parallelism.

The electrical curves were of three types. The first was a slow type, made up of a series of smaller oscillations (12 to 20 to the curve), which more or less corresponded to the mechanical curve. The second type seemed rather to be stimulated by the injection of pituitrin or gynergen. The length in seconds of these different types of curves varied between ten and fifty seconds. In the third type the contractions were between 90 and 110 per minute.

The theory that the human uterus, a relatively large muscular organ, undergoes spontaneous contractions in its nongravid state led us to attempt to verify this by securing permanent tracings of these contractions, using a direct electrical "lead off" from the uterus through the electrocardiograph.

#### TECHNIC OF THE PRESENT INVESTIGATION

Simple electrodes that were easy and safe to apply in the human uterus were constructed (Fig. 1). The lead from the fundus is a slender curved rod of silver, two inches in length, which slips easily into the uterus. It is attached to a long, insulated wire stem, at the other end of which is an adapter for connection with the lead from





As one follows a few women through several months in this manner, a distinct form of movement of the galvanometer string is recognized. These movements occur with a definite periodicity in the cycle (Fig. 3). The waves are irregularly rhythmic.

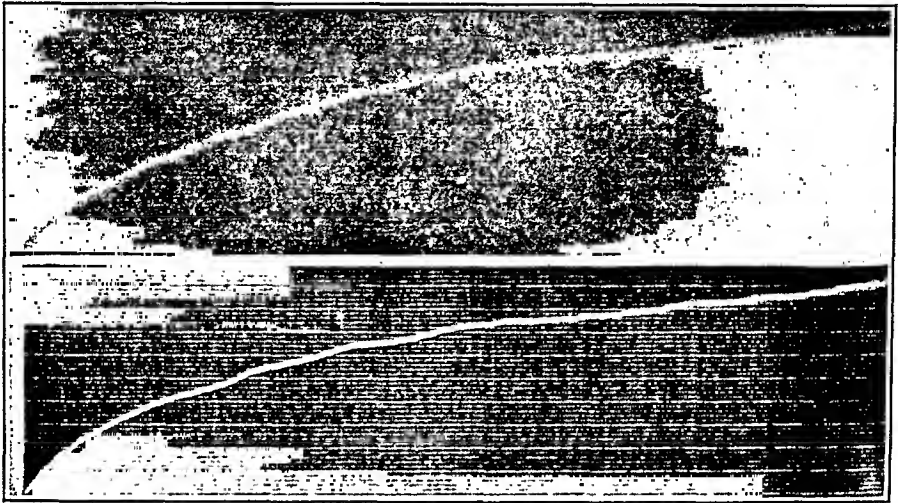


Fig. 4\*.—Almost total absence of string activity. Readings taken A, eight and B, ten days postmenstrual.

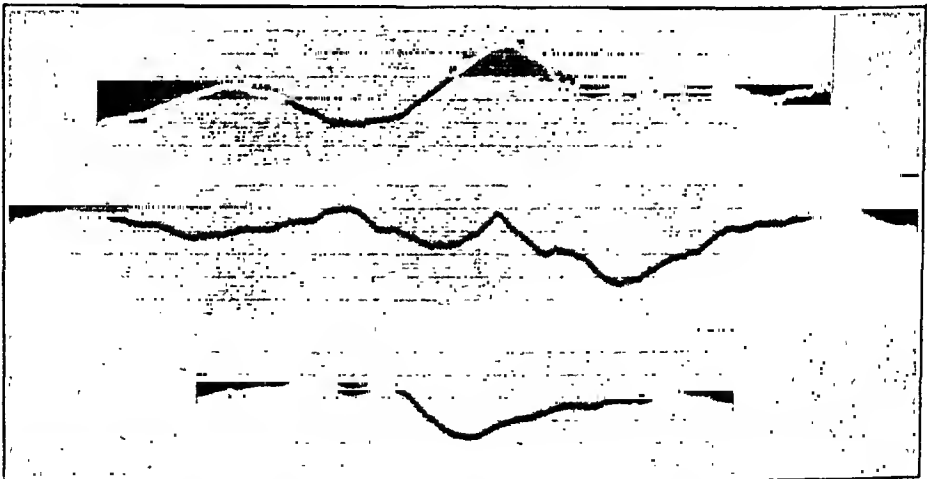


Fig. 5.—String galvanometer activity on thirteenth day postmenstrual.



Fig. 6.—Reading of string galvanometer twenty-third day postmenstrual; no activity.

They differ moderately, one from the other, in duration and intensity. The average length of the wave is about twenty seconds. This, however, varies and waves of as often as three to four seconds and as slowly recurrent as forty seconds have been re-

\*Tracings shown in Figs. 4, 5, and 6 are from the same patient.

corded. When tracings are taken at frequent short intervals, every two or three days throughout the entire month, the contractions begin to appear on or about the ninth day (Fig. 4). They seem to be most marked from the twelfth to the sixteenth day (Fig. 5). They may be present, although diminished, up to the eighteenth or nineteenth day and are rarely found from the twentieth day up to the onset of menstruation (Fig. 6).

Success in demonstrating these waves depends greatly upon the introduction of the inner electrode well into the interior of the uterus and upon the elimination of interfering currents and string wandering.

In the reading of the records obtained there are a number of forms of string activity which must be recognized as artifacts and ruled out.

1. *Artifacts Due to Extraneous Disturbances.*—Slamming of doors, moving of heavy bodies, passing of elevators, and loose electrical connections, produce a series of fine "jiggling" waves which are coincident with that particular disturbance.

2. *Artifacts on the Part of the Patient.*—Strenuous movements of the legs or hips, coughing, straining, sudden very deep breathing and violent peristalsis (as from a recent cathartic), all produce marked irregular deflexions of the string. These disappear with the cessation of the activity.

3. *Pulse Wave.*—Small but definite and regular wavelets occur whose rate is exactly that of the heart. They are superimposed upon whatever other larger waves there may be. One may regard these as a transmission of the cardiac impulse. Against that, however, is the fact that frequently they are entirely absent. It is possible that these small regular wavelets may be in the nature of a "pulse jerk" occurring with uterine engorgement.

4. *Tiny Wavelets.*—Tiny "jiggling" wavelets resembling those of the extraneous causes of known origin mentioned in Group 1, occasionally occur without any perceptible cause.

5. *Wandering of the String.*—In the case of wandering of the string (a phenomenon familiar enough to electrocardiologists) the galvanometer string, when set at one edge of the recording strip, more or less rapidly drifts across the strip and off on the opposite side. It has to be brought back again. While annoying, this wandering does not completely interfere with the registration of the other forms of activity that occur, superimposed upon it. Wandering of the string is commonly attributed to secretions, grease, and impurities at the point of contact of the electrode and the tissues, these being factors which set up interfering surface current. Incidentally, it was thought that wandering of the string occurred at certain periods, the exact definiteness of which could not be determined. An interpretation of this "wandering" led to the belief that there was a more or less periodic change in the reaction of the secretions in the uterine cavity. This would have to be proved by further study.

#### SUMMARY OF OBSERVATIONS

Six patients were followed through a total of fifteen menstrual cycles. One hundred and three readings were taken. As many as nine records were made on one patient during one menstrual interval. The degree of thoroughness with which these cycles were investigated and the number of records made depended upon the cooperation of ambulatory clinic patients and, therefore, varied considerably. In three instances, only two readings could be obtained throughout one entire menstrual interval. While these in themselves would be utterly inconclusive, they can be

interpreted, however, when combined with observations on other menstrual cycles, on the same and other subjects, which were studied more completely.

Eleven menstrual cycles were completely studied on five patients; of these eleven, ten showed a definite increase in string activity from the ninth to the eighteenth day.

The interpretation of the origin of these waves is somewhat problematical. They seem to be of uterine origin. They are much too slow for heart or respiration. They are slow enough for smooth muscle, and there can be no question that they "led off" directly from the uterus. If they represented the muscular activity of an adjacent organ such as bladder, intestine, or colon, one would *not* expect any definite rhythmic cycle of contraction from the tenth to fifteenth day of the cycle. Repeated injections of theelin seemed irregularly to augment these waves. This, too, would argue against the activity of another organ. As these waves occur at the time supposed to be the ovulation period, the waves might be a record of tubal peristalsis. This, however, is very doubtful. Seekinger shows that maximal tubal contractions occur later in the cycle.

If these periodic increases in string activity do represent increased contraction of the uterus, this will be a means, however imperfect, of recording the spontaneous contractions of nonpregnant uteri. Furthermore, as these contractions are apparently coincident with the pressure, if not life, of the developed follicle or the recently expelled ovum, this method may give indirect information regarding stages of ovulation. Theoretically one might explain the absence of contractions up to the eleventh day to a low amount of folliculin, from the eleventh to the twenty-first day ample folliculin, after the twenty-first day the inhibition of corpus luteum.

#### REFERENCES

- (1) *Dickinson, Robt. L.*: Human Sex Anatomy, 1933. (2) *Blair, E.*: Am. J. Physiol. 65: 223, 1923. (3) *Keyes, J. D.*: Bull. Johns Hopkins Hosp. 34: 60, 1923. (4) *Corner, G. W.*: Contrib. to Embryol. No. 64; Carnegie Inst. of Wash. 13: 117, 1921. (5) *Seekinger, D. L.*: Bull. Johns Hopkins Hosp. 34: 236, 1923. (6) *Wislocki, G. B., and Gutmacher, A. F.*: Bull. Johns Hopkins Hosp. 35: 246, 1924. (7) *Brouha, L., and Simonnet, H.*: Arch. internat. de Physiol. 29: 94, 1927. (8) *Wijsenbeek, J. H.*: Nederl. Tijdschr. Voor Geneeskunde 66: 1263, 1922, Reeks-58-1B. (9) *Mikulicz, Radecki F.*: Arch. f. Gynäk. 128: 318 and 361, 1926. (10) *Westman, A.*: Acta obst. et gynec. Scandinav. 5: 1926; Supplement. (11) *Heinricius*: Finska lük.-Sällsk. handl. 31: 349, 1889. (12) *Accanei*: Gior. d. r. Accad. di med. di Torino 39: 497, 1891. (13) *Reynolds, S. R. M.*: Am. J. Physiol. 92: 420, 1930. (14) *Knaus, H.*: Zentralbl. f. Gynäk. 532: 2193, 1929. (15) *Adair, F. L., and Davis, H. E.*: Am. J. Obst. & Gynec. 27: 383, 1933. (16) *Schultze, G. K. F.*: Klin. Wchnschr. 11: 1942, 1933. (17) *Theilhaber, H.*: Monatsschr. f. Geburtsh. u. Gynäk. 31: 727, 1910. (18) *Veit, J.*: Zentralbl. f. Gynäk. 36: 161, 1912. (19) *Blumenfeldt and Dahlman*: Ztschr. f. Geburtsh. u. Gynäk. 75: 493, 1913-14. (20) *Greene, G. W.*: Am. J. Physiol. 85: 376, 1928. (21) *Bode*: Zentralbl. f. Gynäk. 553: 2887, 1931. (22) *Bun-ichi Hasama*: Jap. J. N. Sc. Tr. 5: 67, 1930. (23) *Pozza, F.*: Ann. di Ostet. 55: 603, 1933.

# HISTORICAL REVIEW OF A SYNDROME EMBRACING UTERO- OVARIAN ATROPHY WITH PERSISTENT LACTATION (FROMMEL'S DISEASE)

E. A. SHARP, M.D., DETROIT, MICH.

**A**TROPHY of the uterus and ovaries associated with lactation is a syndrome of historical if not of current interest. Priority of description of this entity appears to have been accorded Richard Frommel<sup>1</sup> of Berlin as a result of his study of 28 cases published in 1882.

It is noteworthy that Frommel, in his essay entitled *Ueber puerperale Atrophie des Uterus*, referred to a description of the syndrome by Chiari in 1855.<sup>2</sup> Two contemporary clinicians, Simpson<sup>3</sup> and Schröder,<sup>4</sup> were cited by Frommel as having been cognizant of the syndrome. Since Chiari might be properly accredited with the initial description of the symptom complex, his original observations will be given in their entirety.

Chiari, with the collaboration of C. Braun and J. Spaeth, published a series of essays on gynecologic and obstetric subjects embracing observations on patients in the clinics of Vienna during the years 1848 to 1855, inclusive. In a subsection of one of Chiari's reports there appears under the title: "Anomaly of size," a description of various types of uteri. In a sketchy, disconnected form of annotation, made more difficult to interpret because of a mixture of archaic, classic, and colloquial idioms, he discussed two cases of puerperal uteroovarian atrophy accompanied by persistent lactation. After commenting briefly on the flaccid, atrophic, and deviated uteri found in chlorotic women, Chiari asserts:

To the acquired uterine atrophies belong two cases described below which were associated with persistent secretion of milk following their puerperiums, causing also complete amenorrhea despite the youthful age of the patients.

the night. Patient also noticed pressure on the breasts caused excretion of a thick, yellow-white milk. On vaginal examination there were revealed an atrophic, prolapsed, lacerated, patent cervix, and a very thin, relaxed uterus of ordinary length.

Chiari comments on these two case histories very briefly as follows:

Leucorrhea (blennorrhea) was not observed in either case before or during the observation. We look upon both as early senile atrophy of the uterus which depends upon the nutritional state of the patient and is more or less influenced by general health.

After reviewing Chiari's brief and informative communication, the failure to recognize the clinical import of the symptom-complex until Frommel's fortuitous essay in 1882 is astonishing at this advanced period.

The opening section of Frommel's essay was devoted to a review of the literature and citations of opinions about the classification, incidence, pathogenesis, and diagnosis of various types of uterine atrophy. Because of his pertinent statistical data and the accurate description of the puerperal syndrome, a slightly abridged translation of his report is subjoined:

Among 3,000 gynecologic patients, 28, or about 1 per cent, showed various types of uterine atrophy. It is of especial interest that atrophy is not limited to women of middle age, who after a great number of pregnancies develop atrophy of the uterus. Of the 28 cases, one patient 19 years of age showed this condition, and the eldest patient in the group was 40 years of age. The average was about 29.6 years. As a rule the women are young and poorly nourished and at first glance do not appear to be in their twentieth year. They come to the physician not because of amenorrhea, despite the fact that breast feeding has been discontinued for several months, but because of a great number of complaints. Abdominal pain, sensations of active movements in the abdomen, backache over the entire back and extending down both legs, and numerous hysterical manifestations are among the symptoms. They are distressed and show mental depression.

The inspection of the external genitalia is, as a rule, negative. No inflammatory changes are present in the uterine adnexa, the ovaries are free and movable, but uterine atrophy is always found. In a few cases the uterus is much smaller, extraordinarily thin, length decreased (5 to 5.5 cm., in one case only 4.5 cm.) and generally firm and palpable. The atrophy affects the cervix, also, which is visible as a small peg in the vagina, or similar to senile atrophy, may be entirely absent. In other cases the uterus is not shortened, but there is a change in the thickness of the walls, so that palpation is often difficult. The uterine body is generally mobile and can be moved from the anteverted to the retroverted position, but this type is usually in the retroposition. The vaginal cervix is often thick and firm but sometimes atrophic and flaccid. In introducing instruments care must be exercised to prevent piercing the uterine walls.

In the majority of cases the ovaries are small and atrophic. Only 3 cases out of 28 showed ovaries of normal size. Menstruation did not reappear in all cases after weaning. In one case the menses resumed for a short time, but amenorrhea ensued. The condition may be caused or at least aggravated by lactation.

Frommel at this point advises breast feeding and describes his findings derived from examination of nursing mothers, concluding that a firm, small uterus is characteristic during lactation. He continues the thesis with these interesting observations on uterine atrophy:

These findings (on normal nursing mothers) support the assumption that in some women, as a result of lactation, the uterus attains such a pronounced degree of involution that a subsequent *restitutio in integrum* cannot occur. This may explain why atrophy is found among women after one or several pregnancies. Atrophy was found in 9 after 6 pregnancies, in 2 after 2, in 6 after 3, in 4 after 4, in 4 after 5, in 1 after 6, in 1 after 7, in 1 after 8 and 1 after 9 pregnancies. In all cases normal menstrual periods were observed.

In one case a young and robust woman developed a marked genital atrophy after her first pregnancy although lactation did not appear. Another woman, 23 years of age, gave birth to a premature baby (6 months) but resumed menstruation three months after delivery, having two scanty periods then ceased for a period of two years. Neither the history nor the examinations disclosed any cause to explain an atrophy of the uterus. A third interesting case was a woman, 28 years of age, who had given birth to five children, the last pregnancy having occurred one and a half years ago. After nursing the baby three months, breast feeding was discontinued, and the menses appeared for three months then ceased completely. Lactation persisted, however, from both breasts so profusely that her underwear and dress were always saturated. This condition continued for one year, and the patient found it necessary to wear two large towels to protect her clothes. Pressure on the breasts expelled an appreciable spray of milk. The uterus was slightly retroposed, 5.5 cm. in length, and thin-walled. Both ovaries were small and atrophic. The condition was still unchanged when this paper went to press.

Frommel concluded that women who experience numerous pregnancies in rapid sequence have imposed on the genital organs a great biologic demand, which may contribute to uterine atrophy. He expressed the belief that the prognosis in genital atrophy due to prolonged lactation was unfavorable, since only one of his 28 cases showed complete recovery. Prophylaxis was recommended—detection of abnormal involution early in the puerperium followed by immediate weaning of the infant. His outline of therapy embraced hot sitz baths, improved nutrition, insertion of pessaries to irritate the uterus, and iron for the anemia.

#### COMMENT

Malnutrition in the inhabitants of the large centers of population in Central Europe during the periods Chiari and Frommel made their observations may have contributed to the incidence of this or any other disease. In any event, the prevalence of the puerperal syndrome was not alarming since less than 1 per cent of three thousand women displayed the same symptomatology.

The rarity of the entity is not so intriguing as its endocrine implications. Mammary function is identified with anterior pituitary control, as is the gonad, while all are physiogenically involved in gestation. A

clear delineation of the mechanism responsible for the precipitate genital changes and persistent postpartum lactation could not be undertaken under any circumstances, however, without data on the antepartum integrity of the ineretory system. Pregnancy alone is presumptive but not conclusive proof of normal balance in the reproductive zone.

#### REFERENCES

- (1) *Frommel, Richard*: Ztschr. f. Geburtsh. u. Gynäk. 7: 305, 1882. (2) *Chiari, J., Braun, C., and Spaeth, J.*: Report of Diseases of Women Observed During the Years 1848 to 1855, Inclusive, in the Department of Gynecology (Municipal Clinic) in Vienna, Klin. der Geburtsh. u. Gynäk., Erlangen (Germany), 1855, Ferdinand Enke, pp. 371, 372. (3) *Simpson, J. Y.*: Diseases of Women, Edinburgh, 1872, p. 597. (4) *Schröder, K.*: Diseases of Women, vol. 4: p. 81 (year of publication not given).

### PREGNANCY COMPLICATED BY CARCINOMA OF THE CERVIX

WILLIAM NEILL, JR., M.D., M.A., BALTIMORE, MD.

(From the Howard A. Kelly Hospital)

THIS report owes its inception to the study of six patients with pregnancy complicated by carcinoma of the uterine cervix met with in this hospital. I propose to present their histories, with the method and results of treatment. Not knowing definitely the viewpoint and practices at other clinics, I have undertaken a review of the literature and, with but few exceptions, found little detail. It consists mostly of observations in one or more individual cases with little or no discussion as to the best method of treatment for this condition as a whole. The vast majority were treated by complete hysterectomy in the earlier months of pregnancy and, after the seventh month, by cesarean section and hysterectomy. Only an occasional instance is reported where radiation alone was used, but considerable advice against such treatment on account of the harmful effect on the offspring. I can find but scanty mortality statistics following the complete operations, but the average of my findings is high.

Fortunately the condition is rare. Stöckel reports that out of 18,000 pregnancies there were 8 cancers of the cervix, or 0.04 per cent. Kerstner's percentage is 0.05 per cent. Hirst in a group of 12,484 pregnancies found only 1 cancer of the cervix, or 0.008 per cent. Gross finds 1 cancer of the cervix in 1,538 pregnancies, or 0.065 per cent. Mendel in 29,962 pregnancies collected from the literature found 24 cancers of the cervix, or 0.08 per cent. In 1,500 pregnancies at the Johns Hopkins Hospital, there were 5 cancers of the cervix, or 0.3 per cent. Among 18,243 pregnancies at the University of Chicago there were two cervical cancers, or 0.01 per cent. In our own material, consisting of 2,703 cancers of the cervix, there were 6 pregnancies, or 0.2 per cent.

The incidence of occurrence is met with in the same relative frequency in primiparas and multiparas as is cervical cancer without pregnancy. The youngest

patient (sixteen years old) is reported by Tuft; an extensive condition ending in death to both mother and fetus without interference at the fourth month. Mylvaganam and Blonstein each reported an instance of twins at term, and Watson, triplets at the fifth month.

There is a divergence of opinion as to whether pregnancy stimulates or inhibits cancer. Such observers as Zweifel and Simpson feel that it increases activity, while Weibel, Wolfe, Meyer, and Stöckel are of the opinion that it retards the growth. On the contrary, Bumm, Hoffmeier, Kobak, and Cullen do not believe there is any effect one way or the other.

The diagnosis should not be difficult. The error frequently made is to consider all abnormal bleeding during the early stages of pregnancy as a threatened abortion and, in the later months, as placenta previa or some type of accidental hemorrhage. The general tendency against making a pelvic examination during pregnancy should be changed, thus preventing an occasional cervical cancer to progress undiagnosed. Much can be learned from a rectoabdominal examination, coupled with a direct inspection. The hesitancy in doing a biopsy undoubtedly is due to its improper performance, the tendency being to remove too great an amount of tissue, necessitating the cautery or suture to check bleeding, with a later possibility of infection. The more simple procedure, fraught with no danger of complication, is adequately accomplished by removing without anesthesia a small bit of tissue with a nasal rongeur forceps from a characteristic area of the erosion with the patient on the office examining table. The patient is able to return at once to her home, and an accurate diagnosis is established.

Considerable has been written as to the effect on the offspring, both where radiation has been given prior to conception and after pregnancy has occurred. In patients treated by radiation followed by a temporary amenorrhea, with a later return of normal menstruation, pregnancy rarely occurs, but should conception take place, there is a marked tendency to miscarriage. Goldstein and Murphy in a study of 650 pregnancies associated with pelvic radiation prior to conception found 24 per cent ended in abortion and 13 per cent in the birth of defective children. From a study of reported cases, it is not clear whether this is a direct result of the radiation, or due to the condition for which the patient was originally treated. It has been definitely determined, however, both by experimentation on animals and from the observation on human beings, that radiation after pregnancy has occurred has a definite tendency to injure the offspring, and because of this, therapeutic radiation during pregnancy should not be carried out unless all other methods of treatment have been carefully considered.

Mendel collected 12 cases from the literature where radiation was used during some stage of pregnancy, with birth by cesarean operation of normal children at term, and 15 others wherein there was definite injury, 4 ending in abortion, 6 at term with



intercranial abnormalities, and 5 malformations. Goldstein in a study of 24 radiated pregnancies reports 16 unhealthy children, and he advises that a pregnant uterus should never be radiated.

It is my opinion that radiation is a much more efficient method of treating cancer of the cervix complicated by pregnancy than any radical operative procedure. The treatment should be instituted just as soon as the diagnosis is made. In the first four months of pregnancy it is hardly possible to radiate without injury to the fetus, and the entire endeavor of the treatment should be directed toward curing the cancer and saving the life of the mother. In the later months it is not only possible to cure the cancer but also to obtain a normal child, by the topical application of radium. It is safe to give in a single application from 3 to 3.5 gm. hours, the technic followed being almost identical with that used in cancer of the cervix not complicated with pregnancy. The patient is placed in the knee-chest posture which, with a Sims speculum, allows full distention of the vaginal cavity and perfect exposure of the entire growth. The radium, held in a cloth form, containing from six to eight separate tubes, is folded over the entire surface. Lead screens are interposed, protecting the bladder and rectum, while the vaginal cavity is packed lightly with sufficient gauze thoroughly to displace all normal mucous surfaces away from the radium. A large amount of radium is used in each instance, the total being from 2 to 3 gm. and the actual time of application is not over one to one and one-half hours, which eliminates any possible dilatation of the cervix that might occur from the packing. We do not place tubes in tandem within the cervical canal to the level of the internal os as is the routine in patients without pregnancy. Careful follow-up examinations are made until after the birth of the child and further treatment given, either through the cervix with radium or externally about the pelvis with x-ray, should it be indicated.

In the early months of pregnancy, should the irradiation not cause abortion after the growth is thoroughly under control, it should be produced by mechanical means. In the later months it is advisable to allow the pregnancy to proceed to term, ending it by cesarean section. The operation should not be any type of a Porro, nor should an attempt be made to remove the uterus. The poor immediate results and high operative mortality from the complete operation would indicate radiation treatment, as outlined, to be the better plan.

#### CASE REPORTS

*CASE 1.—Operable carcinoma of the cervix with pregnancy at the fifth month.* Mrs. M. B., white, aged thirty-two years (No. 22599). Previously she had given birth without difficulty to three children. She was first seen May 13, 1930. There had been irregular vaginal bleeding for the past three months and, prior to pregnancy, a chronic leucorrhoeal discharge. Past history was negative for serious illnesses or operations. On examination, occupying the anterior half of the cervix there

was a large everting, fungating mass, and induration at the base of the right broad ligament, without fixation; left side clear. Hemoglobin was 56 per cent. Child was viable. Tissue diagnosis, squamous cell carcinoma, Grade III. A topical application of radium was given against the growth of 3,109 mc. hours. All bleeding ceased after one week. Next seen July, 1930; pregnancy advancing normally and the cervical growth healed. On Sept. 12, 1930, a normal child, weighing 8 pounds, was delivered by cesarean section. An examination of the lateral pelvic structures intraabdominally revealed no evidence of extension of the growth. In March, 1931, the patient's gallbladder was removed for an upper abdominal condition. Six months after delivery normal menstruation returned and continued until July, 1931, when she was given treatment with x-ray for a total of one E. S. D. over front and back of pelvis to establish an artificial menopause. This was satisfactorily brought about and at present there is no palpable evidence of the carcinoma. The child, four and one-half years old, is perfectly normal.

CASE 2.—*Operable carcinoma of the cervix with pregnancy at the sixth month.* Mrs. A. W., white, aged twenty-nine (No. 24792). First seen Nov. 28, 1931. Past history negative for serious illnesses or operations. She had two living children and two miscarriages. Chronic leucorrhea had been present for years. First noted irregular bleeding in January, 1931, four months before pregnancy occurred and continued in scanty amount without cessation until August, 1931, when the bleeding increased and treatment was instituted for threatened abortion. On examination there was a friable bleeding mass on the posterior cervix; no lateral extension. Tissue examination, squamous cell carcinoma, Grade III. A topical application of radium was applied against the cervix for a dosage of 3.6 gm. hours. Labor began Feb. 11, 1932, when a cesarean operation was done with the delivery of a normal 8-pound baby. At the time of operation palpation within the pelvis failed to reveal any evidence of intrapelvic malignancy, and the cervix was healed. Jan. 19, 1935; mother and child both healthy; no evidence of any cancer. Normal menstruation occurred six months ago and has been regular ever since. X-radiation over the pelvis for an artificial menopause was advised which so far has been refused.

CASE 3.—*Operable carcinoma of the cervix with pregnancy at seven and one-half months.* Mrs. O. H., colored, aged twenty-eight (No. 17355). First seen Dec. 1, 1926. Past history was negative as to serious illnesses or operations. There had been four normal pregnancies. Scanty vaginal bleeding began in September, 1926, which was continuous until I saw her, and during this period, she was treated for threatened abortion. Health continued good and she gained in weight as the pregnancy advanced. On the right side of the cervix was a solid, nonulcerating, rounded tumor, bleeding on touch. The cervix was movable with the fundus, and the fornices were clear. The tumor, with the cervix, could be delivered entirely outside the vagina, and was removed with the cautery. Tissue revealed squamous cell carcinoma, Grade III. On Dec. 15, 1926, four glass radon capsules, each containing 2.5 mc., were implanted permanently into the cervical stump and on Dec. 18, 1926, 1,765 mc. of radon topically applied. The pregnancy continued its normal course, with cessation of bleeding, until Jan. 16, 1927, when her first labor pains began and a healthy female child, weighing 6 pounds, 4 ounces, was delivered by cesarean section. On April 1, 1927, a superficial but definite metastatic nodule 1 cm. in diameter was removed from the right vaginal orifice with the cautery. The patient remained well without return of menstruation until January, 1931, when there was a definite mass in the right femoral region, the pelvic structures remaining perfectly clear. In May, 1931, there was a profuse hemorrhage from this sloughing mass, occurring at her isolated home in the country, and she died before a physician could reach her. The child is well and over eight years of age.

CASE 4.—*Extensive, inoperable carcinoma of the cervix with pregnancy.* H. M., colored, aged thirty-eight (No. 24279). First seen on June 5, 1931. She had three normal children; one miscarriage. There had been no complication with the present pregnancy until the fourth month, when a scanty, irregular, bloody vaginal discharge appeared which continued. For years there had been a chronic leucorrhea. Past history was negative for serious illnesses or operations. On examination, cervix occupied by a large, craterous ulceration, with involvement in the right broad ligament region all the way to the pelvic wall, and to a lesser extent on the left. Tissue diagnosis: squamous cell carcinoma, Grade III. A cesarean section was done the following day, with delivery of a normal child. On July 12, 1931, a topical application of radium was given against the cervix of 3,000 mc. hours, and a series of deep x-ray treatments through multiple portals about the pelvis, completed July 30, 1931. Sept. 27, 1931, the condition was no better. Sept. 30, 1931, one gold radon capsule, 13.6 mc., was implanted permanently into the cervical growth, and on Nov. 15, 1931, an additional 1,000 mc. hours applied against the cervix. There was little, if any, general improvement, but definite relief from pain and hemorrhage. Death occurred from the disease on April 23, 1932.

CASE 5.—*Extensive carcinoma of the cervix with pregnancy at term.* Neglected for one and one-half years. Mrs. E. F., white, aged thirty-nine (No. 24280). Past history was negative as to serious illnesses or operations. She had six children; two miscarriages. On Dec. 10, 1929 she was delivered elsewhere of a normal child by cesarean section followed by supravaginal hysterectomy. On account of irregular bleeding, while in the hospital, the cervix was examined and tissue removed, which revealed squamous cell carcinoma, Grade III. No attempt was made to do anything for this condition and she was discharged. The bleeding continued in small amounts without symptoms until September, 1930 when it became profuse and she consulted another physician and was told she had change of life, and nothing was done until July, 1931 when, due to the continuation of bleeding, she was sent to this hospital. On examination cervix was replaced by a huge, fungating mass, nearly filling the vaginal cavity, with complete fixation from side to side. Palliative x-ray treatment given July 25 and 26, and on August 3, 3,000 mc. hours radium radiation given against the cervix. This checked the bleeding and made the patient more comfortable, but she died of the disease on Sept. 4, 1931.

CASE 6.—*Extensive carcinoma of the cervix with pregnancy, spontaneously delivered at term.* Mrs. T. K., white, aged thirty-five (No. 23125). Past history negative for serious illnesses or operations. She had ten children. Suffered from chronic leucorrhea for years. In April, 1930 at the fifth month of pregnancy there appeared an irregular bloody vaginal discharge. On Aug. 24, 1930 she was delivered spontaneously, with considerable difficulty and hemorrhage. The baby lived three days, its death being due to a malformation of the esophagus. Nothing further was done, the opinion being that the condition was hopeless. Due to pain and bleeding I was asked to see her on Sept. 30, 1930. On examination patient was pale and ill and the vaginal cavity almost entirely filled with a large, fungating growth, with fixation to both broad ligaments and base of the bladder region. On Oct. 2, 1930 the large fungating mass was removed with a dull spoon curette, and it was felt that she would develop a vesicovaginal fistula. Tissue diagnosis: squamous cell carcinoma, Grade III. On Oct. 4, 1930 a topical application of radium was given against the growth for a dosage of 3,000 mc. hours. Astonishing improvement immediately followed and in July, 1931 everything was healed at the vaginal vault, but there was still fixation laterally. On July 18, 1931 an additional 1,000 mc. hours radium radiation was given against the vaginal vault for a recurrent ulcer, showing active

cancer. She remained symptomatically well until December, 1933 when extensive recurrence was noted locally and 1,400 mc. radium hours were given against the recurrence, checking the bleeding and affording comfort to the patient, but her general condition declined, and a vesicovaginal fistula developed in February, 1934, which persisted until her death of the disease in July, 1934.

## REFERENCES

- Muller*: Hand. der Geburt. 1889. *Gallen*: Cancer of the Uterus, New York, 1900, D. Appleton-Century Co. *Spencer*: Proc. Med. Soc. of London, 1920. *Mendel*: AM. J. OBST. & GYNEC. 13: 86, 1927. *Ibid.* Bunim, Hoffmeier, Koblack, Sommers, Weibel, Warf, Mager, Fullner. *Neill*: AM. J. Roentgenol. 17: 461, 1927. *Stern*: AM. J. Roentgenol. 19: 133, 1928. *Bowman*, *ibid.* *Martin*, *ibid.* *Murphy*: Surg. Gynec. Obst. 47: 201, 1928. *Kane*: Virginia M. Monthly 55: 308, 1928. *Condamin*: Gynecologie 27: 577, 1928; Bull. Soc. d'obst. et de gynéc. 17: 862, 1928. *Murphy and Goldstein*: AM. J. OBST. & GYNEC. 18: 179, 1929; AM. J. Roentgenol. 22: 207, 1929. *McGlinn*: AM. J. OBST. & GYNEC. 18: 592, 1929. *Tuft*: Arch. Path. 9: 654, 1930. *Kaplan*: AM. J. OBST. & GYNEC. 17: 654, 1930. *King*: China M. J. 44: 667, 1930. *Falarde*: Semaine méd. 2: 770, 1930. *Bloomstein*: Lancet 2: 903, 1931. *Stöckel*: Ztschr. f. Geburtsh. u. Gynäk., p. 101, 1932. *Harris*: AM. J. Roentgenol. 27: 415, 1932. *Neilson*: Acta obst. et. gynec., Scandinav. 13: 225, 1933; 14: 1037, 1933. *Burnam*: Curtis Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders & Co. *Herand*: Rev. méd. Peruana 5: 1048, 1933. *Lancier*: Rinase. med. 10: 134, 1933. *Crousse and Ancicux*: Surg. J. Brussels 35: 8, 1934. *Van Rooney*: J. Obst. & Gynec. Brit. Emp. 41: 404, 1934. *Soronia*: Riv. Son. Siciliana 22: 284, 1934. *Sage*: Nebraska M. J. 19: 140, 1934. *Buckley*: J. Obst. & Gynec. Brit. Emp. 41: 402, 1934. *Miller*: New England M. J., p. 402, 1934. *Westman*: Acta Obst. et Gynec., Scandinav. 14: 191, 1934.

---

Mitsui, K.: A Study of Appendicitis in Gynecology, Jap. J. Obst. & Gynec. 17: 291, 1934.

Mitsui studied 230 appendices removed during the course of gynecologic operations. He found a stricture of the appendix in 24 cases. There was evident decrease in the mobility of the cecum in 27 cases, and 25 of these had complicating appendicitis. There was excessive mobility of the cecum in 17 cases and only 8 of these had associated appendicitis. The author found bacteria in 91 per cent of all the appendices; he also studied the tubes and ovaries of 53 of these cases and found bacteria in 19 of them. He failed to find any direct connection between the lymphatics of the appendix and the female genitalia as claimed by Clado and Durand.

In the series of 230 cases, the appendix was found diseased in 143 cases. Hence there is a definite relationship between appendicitis and gynecologic disease. Cystic degeneration of the ovaries occurred in 30 per cent of the cases. Furthermore, 53 per cent of all these patients were sterile, hence there is a definite connection between sterility and appendicitis. In addition, there were 21 cases of ectopic pregnancy, 8 of which complicated appendicitis.

The author believes that when women of marriageable age have an attack of appendicitis the appendix should be removed even if the attack is slight.

J. P. GREENHILL.

## TUBERCULOUS ENDOMETRITIS

MARTIN W. DIETHELM, M.D., A.M., F.A.C.S., AND  
THOMAS L. RAMSEY, M.D., C.P., TOLEDO, OHIO  
(*From St. Vincents Hospital*)

**T**UBERCULOSIS of the female genital tract is in itself not as common as generally supposed. Tuberculosis of the endometrium, diagnosed as an isolated lesion from the uterine curettings without demonstrable pathology in the tubes or in the cervix, can safely be assumed to be an uncommon lesion.

In the Department of Pathology of our hospital, receiving approximately 4,000 fresh tissues from the surgical service each year, among which there is a yearly average of about 500 gynecologic specimens, tuberculosis of the genital tract has been found only thirty times during the last seven years, or in about 0.85 per cent. Tuberculosis in the endometrium has been observed but once.

Dickinson<sup>1</sup> is of the opinion that most lesions are secondary and descending and that the endometrium is involved in about 40 per cent of genital tuberculosis. Gupta<sup>2</sup> believes that when the corporeal endometrium is involved the tubes are nearly always infected. He states that tuberculous endometritis is rarely diagnosed clinically because of the difficulty of demonstrating the bacillus in the discharges, and he prefers curettement for differential diagnosis. He reported six cases of cervical and corporeal tuberculosis, two of which seemed to be primary in the cervix. Reinhart<sup>3</sup> found tuberculosis comparatively rare in genital pathology. He cites Fromme and Heynemann who found genital tuberculosis in 142 of 17,470 autopsies, or about 0.81 per cent and Schlipfert who found 3.4 per cent of genital tuberculosis in tuberculous women and children. Reinhart reports two cases.

The infrequency of endometrial involvement has been explained by some writers as due to the physiology of the uterus with its periodic desquamation, making bacterial rests difficult of maintenance. This is questionable as the mucosa does not entirely desquamate during menstruation. Trauma, previous infection, and pathologic changes interfering with the menstrual function are credited as being etiologic factors. Clinical symptoms, unless associated with frank tuberculosis elsewhere, when the diagnosis can be made by inference only, are not particularly illuminating: nor are the findings on examination. Demonstration of the microorganisms or the characteristic tubercles in uterine curettings or in cervical biopsies seems to offer the only certain means of diagnosis previous to generalized pelvic tuberculosis calling for laparotomy.

### CASE REPORT

Mrs. P. C. G., aged twenty years, white, one child, one miscarriage. There were three admissions to the hospital. Jan. 15, 1933: She was admitted by her physician for incomplete abortion. Her pregnancy was of two months' duration. There was no intrauterine manipulation, and after spontaneous evacuation, the patient was sent home cured. On Aug. 23, 1933, she was again admitted complaining of menorrhagia and dysmenorrhea. The periods were of twelve days' duration and excessive in amount with some premenstrual discharge. Her past history revealed pneumonia, diphtheria, tonsillectomy, and appendectomy. Her general health had

been good and she had been leading a very active social and athletic life. Weight about seventy-two pounds. Height five feet two inches. A careful pelvic examination showed a small, firm, freely movable uterus, normal in contour, and in good position. The adnexa were not palpable nor tender. There was a slight cervical erosion with bilateral laceration of the cervix and some hypertrophy. The introitus was parous, and the perineum in good condition. No lesions were noted on the vulva or the vaginal mucous membrane. The urine was negative except for an occasional pus cell. The blood showed hemoglobin 69 per cent, R.B.C. 3,350,000, W.B.C. 6,450; polymorphonuclears 66 per cent, lymphocytes 30 per cent, monocytes 3 per cent, transitionals 1 per cent. Wassermann and Kahn negative. Metabolism reading was -9.

A diagnostic curettement was done and microscopic examination of the curettings showed numerous typical tubercles as well as the tubercle bacillus.

A roentgen examination of the chest showed the chest symmetrical, heart somewhat rounded, hilus shadows increased, increase in the linear markings on both sides, most marked on the right side with a suspicious area in the second interspace posteriorly on the right. However, this did not appear active.

The pulse, temperature, and respiration range remained normal. She was discharged on the seventh day with the diagnosis of miliary tuberculosis of the endometrium. The condition was explained and extirpation was advised, but was refused by the patient and her husband on the grounds of comparative health and lack of convincing discomfort.

Oct. 10, 1933, admitted for hysterectomy. Following her discharge in August there had been almost daily bloody discharge. General health was good until one week ago, when there was abdominal pain of dull character radiating down the legs, made worse on standing and on walking. She also had a "cold," with coryza and slight cervical adenopathy. Physical examination was much the same as on previous examination except for the pelvic findings, and here a great change was observed. The uterus was fixed in the pelvis. There were bilateral tender masses fairly soft in consistency. The cervix was little changed, the erosion being about the same. The temperature, pulse and respiration range were normal. The urine showed traces of albumin and few pus cells. The hemoglobin was 87 per cent, R.B.C. 4,510,000, W.B.C. 9,550. A diagnosis of pelvic tuberculosis was made, and a complete hysterectomy with bilateral salpingo-oophorectomy done (M. W. Diethelm).

The peritoneum was found studded with tubercles. There was a small amount of pale fluid in the pelvis, and the uterus and adnexa were bound down by an exudate and recently formed adhesions. The tubes were large, thickened, and tortuous. Both ovaries were cystic. The uterus, cervix, tubes, and ovaries were removed.

TABLE I. SHOWING TUBERCULOSIS FOUND IN GYNECOLOGIC SPECIMENS EXAMINED IN ST. VINCENTS HOSPITAL PATHOLOGICAL LABORATORY DURING THE LAST SEVEN-YEAR PERIOD\*

	1927	1928	1929	1930	1931	1932	1933	TOTAL
Tuberculous specimens	2	10	3	5	3	3	4	30
Tubes only	2	7	2	4	2	3	3	23
Tuboovarian		3	1		1			5
Ovarian only								0
Tubes and broad ligament				1				1
Endometrium								0
Cervix, tubes and endometrium							1	1
Total number gynecologic specimens	501	558	603	507	578	477	423	3647

\*Percentage of tuberculosis found 0.85.

en masse, and the vagina and abdomen were closed without drainage. Convalescence was uneventful except for an allergic reaction to luminal. She was discharged on the twenty-first day. She has been examined twice since the operation and the pelvis is free from induration, masses, or tenderness. She is in good health and has

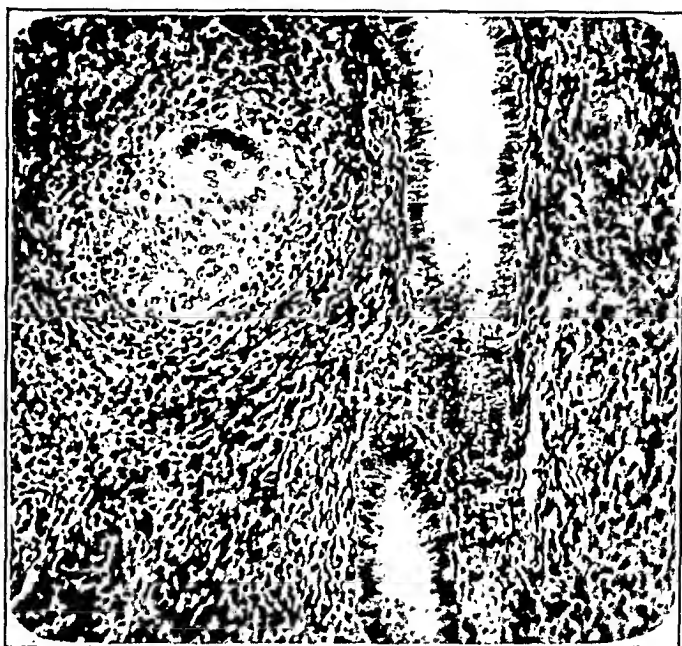


Fig. 1.—Microphotograph showing typical tubercle as seen in curettings for diagnosis.  $\times 100$ .

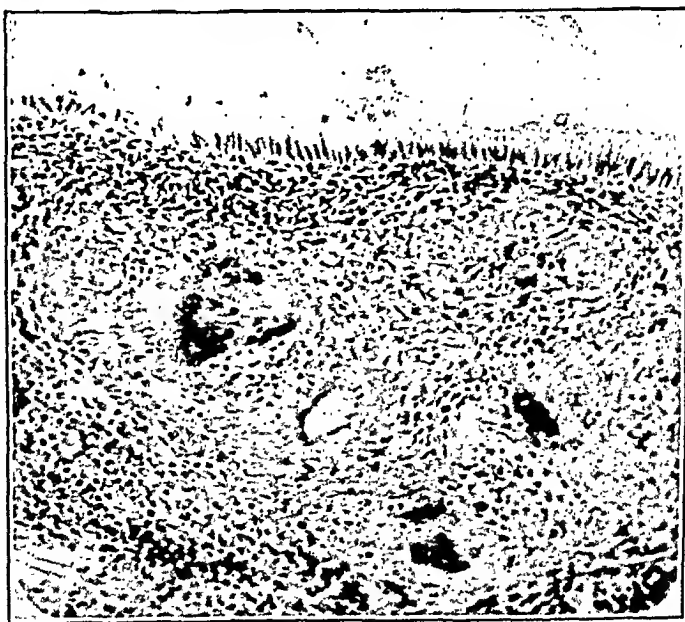


Fig. 2.—Microphotograph, cervix after hysterectomy showing coalescing tubules in stroma between gland crypts.  $\times 100$ .

gained some 34 pounds. Her physician reported in October, 1934, that she is apparently cured.

The specimen was examined grossly and microscopically and microphotographs made (T. Ramsey), the description of which follows:

*Gross.*—The specimen included the uterus, cervix, both tubes, and both ovaries. The cervix was small, rather irregular in shape and showed erosion at external os. The mucosa of the canal was thickened and congested. The uterus was small, measuring 8 cm. in length by 4 cm. across the fundus; the wall showed a moderate fibrosis; the

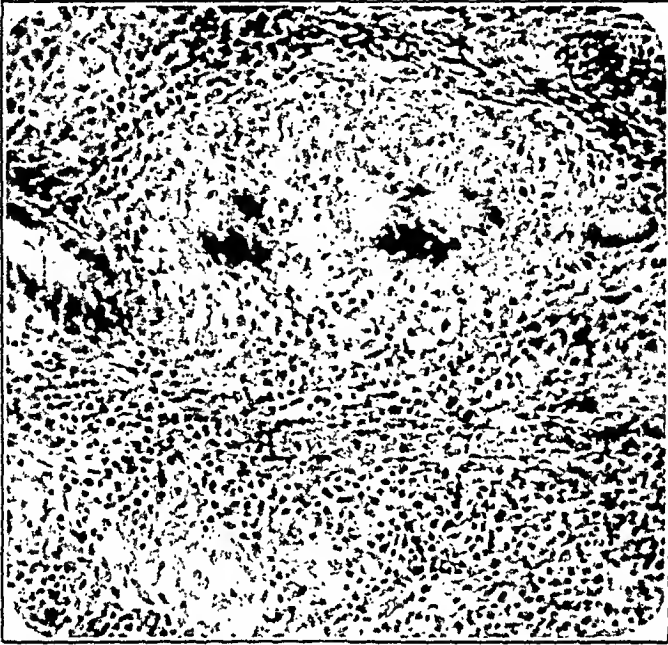


Fig. 3.—Microphotograph showing tubercles in residual endometrium after curettage. Sections taken following hysterectomy.  $\times 100$ .



Fig. 4.—Microphotograph showing tubercle in thickened folds in fallopian tube.  $\times 100$ .

endometrium was edematous and appeared to be thickened especially in the fundus. The tubes were constricted at the uterine ends and were markedly congested, the largest measuring about 16 cm. in length by  $2\frac{1}{2}$  cm. in diameter at the fimbriated end which was occluded. The other tube was very tortuous and measured 11 cm. in



length. Upon cutting into the tubes, they were seen to be distended with pus which was of a thick yellow consistency. The tubal ligaments were thickened. The ovaries were enlarged and partially destroyed by multiple cyst formations. The peritoneal surfaces of both tubes and ovaries appeared somewhat granular. There was a granular appearance on the peritoneal surface of the fundus uteri. Sections were taken from the cervix, fundus of the uterus, and from the ovaries and tuboovarian ligaments.

*Microscopic.*—The cervix showed chronic ulceration at external os with considerable scar tissue formation. The exposed surfaces showed round cell infiltration and a few tubercles in the granulation tissue. The uterus showed fibrosclerosis, and the mucosa was thickened and contained numerous actively developing tubercles with epithelioid and giant cells. The glands were irregular and somewhat distended, forming small cysts. The tubes showed dense infiltration with inflammatory cells, and the folds were thickened and filled with developing tubercles, practically obliterating the tubal lumen. The tuboovarian ligament was thickened and showed productive inflammation with numerous tubercles. The ovary was cystic and sclerotic. No tubercles were seen in the ovarian substance or developing upon its surface. The peritoneum over the tubes, ligaments, and fundus of the uterus showed developing tubercles in and upon its surface.

*Diagnosis.*—Active tuberculosis involving the cervix, endocervical mucosa, mucosa of the uterus, folds and walls of the tubes, tuboovarian ligaments, and peritoneum over the surface of the pelvic organs. The ovaries were uninvolved but showed fibrosis and cystic degeneration. Tubercle bacilli were found in the giant cells.

*Comment.*—This case is presented because of its unusual features, and because of the rarity of tuberculous endometritis. Our impression is that it is an ascending infection, and primary in the cervico-uterine canal extending after curettement to the pelvis. We are led to believe that by careful and perhaps by repeated curettements preferable during the midinterval period, a differential diagnosis can be made. An early diagnosis with complete hysterectomy would anticipate the pelvic extension and allow the conservation of the ovaries in the ascending type. It would seem that since the tubes are so quickly involved, they should always be removed with the uterus even if not visibly affected. In our case the interval between the initial diagnosis, when operation was advised, and the time when the subjective symptoms forced the acceptance of surgical relief, was but six weeks. The pelvic touch picture changed from apparently negative to one simulating the so-called "frozen pelvis."

#### REFERENCES

- (1) Dickinson, Arthur M.: Am. J. Surg. 11: 558, 1931. (2) Gupta, N.: Indian Med. Gazette 63: 304, 1928. (3) Reinhart, Harry L.: J. Lab. & Clin. Med. 14: 413, 1929.

---

Schumacher, P. H.: The Question of Periodic Infertility in Women, Monatsschr. f. Geburtsh. u. Gynäk. 99: 64, 1935.

From a study of the literature and from his own investigations, Schumacher comes to the conclusion that Ogino and Knaus are wrong when they maintain that women cannot possibly conceive during the few days of the premenstrual period. Schumacher firmly believes that the premenstruum is not an absolutely safe period but only a period when conception takes place with more difficulty than at other times in the menstrual cycle. He reports three carefully controlled cases which support his contention and oppose the belief of Ogino and Knaus.

J. P. GREENHILL.

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.

MASSIVE COLLAPSE OF LUNG FOLLOWING CESAREAN  
SECTION

G. W. GUSTAFSON, M.D., F.A.C.S., INDIANAPOLIS, IND.

*(From the Department of Obstetrics, Indiana University Medical School)*

POSTOPERATIVE massive collapse of the lung or atelectasis was first described as a clinical entity by W. Pasteur in 1910. In 1925 Scott reviewed all cases then reported, which were 64 in number. Of these 64 cases, only 38 were given in sufficient detail to permit analysis. Since this time many cases have been reported, chiefly by general surgeons, internists, radiologists, and bronchoscopists. Several of the reported cases have followed gynecologic operations. I noted one case of partial collapse following a cesarean section by Piper of Philadelphia, reported by Chevalier Jackson and Lee. This patient died on the third day, and autopsy showed postoperative collapse of the left lower lobe of the lung, partial atelectasis of base of right lobe with terminal localized peritonitis and paralytic ileus.

Collapse or atelectasis has developed in patients on whom operations had been performed under ether, nitrous oxide-oxygen, spinal, and even under local novocaine anesthesia. The purpose of the following report is to focus attention to its occurrence, diagnosis, and course, in the hope that we as obstetricians and gynecologists will permit fewer cases to go unrecognized.

CASE REPORT

M. C., a twenty-three-year-old primipara, first consulted me on Nov. 16, 1933. Menses had started at fourteen, had been very irregular and accompanied by considerable dysmenorrhea. Her last period began July 23, making her due April 30. Her father had died of pneumonia, and her mother, one sister, and one brother were living and well. She had had measles, whooping cough, a tonsillectomy, and an appendectomy. About a year ago, she had had insertion of a stem pessary for dysmenorrhea by a general surgeon. General examination was negative. External measurements were 25:27:32:19 and bi-ischial 9. Internal examination revealed a four months' pregnancy with no adnexal pathology. The promontory was rather easily reached, her C.D. measuring 12 cm. and C.V. estimated at 10.5 cm. Her entire prenatal course was uneventful with all findings within normal limits, until on April 12 she reported with a severe cold of a week's duration. I immediately sent her to her rhinologist for treatment, a measure strongly advocated by Lubin as prophylaxis against massive collapse. On April 20, 1934, she seemed well over her infection.

On April 25 the patient entered the Methodist Hospital with contractions every two to three minutes. These stopped at 4:00 A.M. on April 26, and active labor started at 11:00 P.M. on that date. After fifteen hours of trial labor, a cesarean section was advised because of disproportion. There was marked overriding of the head which was fixed, but not engaged, and could not be "impressed" to the spines, the baby being large and the pelvis slightly flat. The conditions present were: (1) patient in labor for fifteen hours, (2) B.O.W. intact, (3) fetal heart 144, (4) position O.D.T., (5) station—1, (6) dilatation 7 cm.

The patient refused local anesthesia. Her preanesthetic medication was sodium amytal gr. 6 and atropine sulphate gr. 1/150. A low cervical cesarean with transverse incision in the lower uterine segment was done, under nitrous oxide-oxygen anesthesia, given by a trained anesthetist of many years' experience. Morphine sulphate gr.  $\frac{1}{6}$  was given after the birth of the baby. The latter was a 9-pound boy. The patient was in good condition throughout the operation though she had a moderate amount of mucus. On waking she had some desire to cough. Her position was changed frequently, and the next day she continued to cough up thick mucus. On April 29, 1934, the patient complained of a feeling of compression in the upper chest and was coughing and expectorating thick pus. Her highest temperature had been 101.6° F., pulse 120, and respirations 24. On auscultation of the chest there were few breath sounds over the right chest, while those of the left were exaggerated. She was seen at 10:30 A.M. that day by her internist, Dr. Edgar

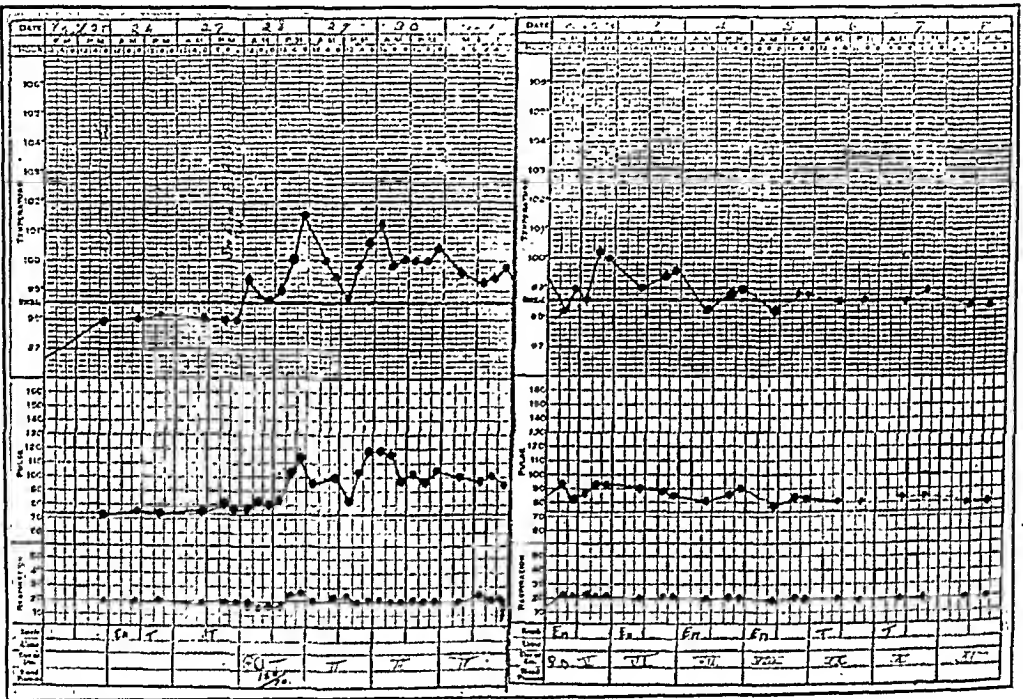


Fig. 1.—P. T. R. curves.

Kiser, who found dullness and impaired breath sounds over the right lung, posteriorly, and upper right lung, anteriorly. There were increased breath sounds over the left lung. At 8:30 P.M. there was complete absence of breath sounds over the entire right lung with the apex impulse of the heart in the midsternal line. Slight cyanosis was noted. With these findings, Dr. Kiser made a clinical diagnosis of atelectasis or massive collapse of the right lung. Symptomatic and postural treatment, as outlined by Sante, was decided upon.

Thick greenish pus was expectorated by the patient until May 3, and was usually the result of paroxysms of coughing. Blood counts were as shown in Table I.

Progress of the patient can best be shown by the P.T.R. curves (Fig. 1) and the roentgenograms taken at her bedside. The first one taken on April 29, 1934, is shown in Fig. 2. This demonstrates a gross pathologic change on the right side, characterized by obscuration of the right leaf of the diaphragm, and a smooth, homogeneous density over the entire right chest. The interspaces between the upper ribs appear to be definitely narrowed as compared with those on the opposite

side. The left lung is entirely clear, with the exception of an old primary healed specific focus in midlung field. The roentgenologist concurred in the diagnosis of atelectasis.

The second roentgenogram was taken on May 1, 1934 (Fig. 3). The right leaf



Fig. 2.—Roentgenogram taken on April 29, 1934.



Fig. 3.—Roentgenogram taken on May 1, 1934. Fig. 4.—Roentgenogram taken on May 4, 1934.

of the diaphragm is markedly elevated, its position corresponding to the sixth interspace, posteriorly. The left occupies a position at the level of the ninth interspace. There is a gross pathologic change in the right chest characterized by marked increase in density involving the right lung. The left lung is clear. In comparison

with the study of Apr. 29, 1934, there is a very marked change in the appearance of the right chest. The right lung, previously entirely obscured, now appears partially aerated; the right leaf of the diaphragm, previously obscured, is now visualized.

TABLE I

	4/27/34	4/30/34	5/9/34
Hg.	60% or 11.2 gm.	58% or 11 gm.	67% or 11.3 gm.
Red count	3,380,000	2,990,000	3,260,000
White count	10,850	8,750	17,000
Polymorph	74	91	76
Eosinophiles	0	1	2
Basophiles	0	0	0
Small lymphocytes	25	8	10
Large lymphocytes	0	0	5
Mononuclears	1	0	1
Myelocytes	0	0	5
Polys			
Band	4	4	0
Bilobed	0	3	0
Adult	96	93	100

The third roentgenogram was taken on May 4, 1934 (Fig. 4). In comparison with the study of May 1, there has been marked clearing of the previously described atelectasis of the right lung. The right leaf of the diaphragm, previously at the level of the sixth interspace posteriorly, is now at the level of the eighth rib. The cardiac and supracardiac shadows are still slightly retracted to the affected side. The left lung remains clear.

The patient continued to improve, and mother and baby left the hospital on May 11, 1934, in good condition. At the present time the patient seems to have made a complete recovery.

#### COMMENT

This case has shown the most typical findings and course in atelectasis. Prophylaxis should include treatment of sinusitis and oral infection, partial Trendelenburg position while operating, removal of mucus by suction, frequent change of position postoperatively along with carbon dioxide inhalations, and the wider adoption of local anesthesia. When the condition occurs, prognosis is favorable unless a pneumonic process develops. The majority of patients do well with expectant, symptomatic, and postural treatment. CO<sub>2</sub> inhalations are advisable. Occasionally bronchoscopy may be indicated. Atelectasis probably occurs more often than we realize, both postoperatively and in the puerperium.

#### REFERENCES

- Pasteur, W.*: Lancet 2: 1080, 1910. *Scott, W. J. M.*: Arch. Surg. 10: 73, 1925. *Jackson and Lee*: Ann. Surg. 82: 364, 1925. *Lubin*: Am. J. Surg. 19: 80, 1933. *Sante*: J. A. M. A. 88: 20, 1927. *Scrimger, F. A. C.*: Surg. Gynec. Obst. 32: 486, 1921. *Scrimger, P.*: Lewis' Practice of Surgery, Vol. 5. *Faulkner, W. B., and Faulkner, E. C.*: Northwest Med. 32: 87, 1933. *Eliason, E. L., and McLaughlin*: Surg. Clin. North America 14: 1, 1934.

## AN INSTANCE OF LIKE MONSTERS IN SUCCESSIVE PREGNANCIES

M. G. DERBRUCKE, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics, Coney Island Hospital)

LIKE monstrosities occurring in successive births to the same mother, in whom were manifest some of the malformations found in the offspring, is a fact clinically as well as embryologically significant.

L. G., aged twenty-three years, primipara, was admitted to the hospital Mar. 1, 1932. After seventeen hours of active labor, she spontaneously delivered an eight-month, well-developed, female infant, weighing 4 pounds 7 ounces. It lived approximately twenty-four hours. The mother had a harelip, cleft palate, and no nasal septum. These had been reconstructed. She had a justominor pelvis.

*Autopsy.*—There was considerable molding of the head. No nasal septum, there being a single, external nares. The left eye was larger than the right. On opening the skull, about 15 ounces of clear fluid were obtained. The brain tissue consisted of a frontal lobe, collapsed, in the anterior part of the skull. The posterior and superior portions of the cerebrum were missing. The ventricles were not covered with brain tissue. The convolutions of the frontal lobe were diminished in number and the medulla showed marked congestion of the blood vessels. The other findings were normal.

*Diagnosis.*—Porencephaly; congenital absence of nasal septum; left eye larger and more prominent than right; prematurity.

The patient was readmitted Feb. 24, 1933, about one year after the delivery of the first monstrosity. Her last period, she claimed, was Apr. 12, 1932, due Jan. 19, 1933. This made the pregnancy five weeks postmature—in a woman with a justominor pelvis. X-ray examination showed a marked disproportion between fetal head and maternal pelvis. These factors were considered sufficient indication for section. The infant, another female, lived several hours.

*Autopsy.*—The body was that of a white, female infant, 51 cm. long, weighing 8 pounds, with the head distinctly enlarged, and prominent frontal eminences. The eyes were sunken and very soft, set close together, being 1.5 cm. between the inner and 5 cm. between the outer canthi. The nasal septum was absent, there being a single central nostril. The fontanels were widely open, the sutures gaping, readily admitting one to one and one-half fingers.

On opening the skull through the sutures, about 700 c.c. of clear, colorless fluid escaped. The brain was compressed downward and anteriorly so that it occupied but a small portion of the cranial cavity. The cerebral hemispheres were represented by a thin sheet of homogeneous, yellowish white material, measuring 0.5 cm. in thickness. The corpus callosum could not be made out. The two ventricles appeared as one large, circular opening, 3 cm. in diameter, communicating directly with the fluid noted subdurally. The third ventricle could be probed. The cerebellum was intact and of normal development, likewise the pons, the medulla, and the spinal cord. The optic nerves showed a normal chiasmie arrangement and ended in the small eyes above noted. The other organs were normal.

*Diagnosis.*—Porencephaly; hydrocephaly; maldevelopment of cerebral hemispheres; absence of nasal septum; close approximation of eyes; enophthalmos.

Two cases of porencephaly, with maldevelopment of the cerebral hemispheres, structural defects in the eyes, and absent nasal septums, occurring in successive pregnancies to the same mother, who, likewise had a deficient nasal septum, besides a harelip and cleft palate, are worthy of note. Clinically, at least, such an occurrence of so closely related malformations seems to point to a germ plasm defect, transmitted through the ova.

901 WASHINGTON AVENUE

## A CASE OF CHONDRODYSTROPHIC NANISM WITH DELIVERY BY CESAREAN SECTION

L. A. BALASQUIDE, B.S., M.D., F.A.C.S., PONCE, PUERTO RICO

(From the Obstetrical and Gynecological Service, Dr. Pila's Surgical Clinic)

CHONDRODYSTROPHIC nanism also called chondrodystrophia fetalis (Kaufmann), achondroplasia (Parrot), chondromalacic micromelia (Kirehberg) is a congenital disease of the skeleton productive of a peculiar type of dwarfism which, according to Bangson, is "due to a defect in the formation of cartilage on the ends of the long bones." After this arrest of development of the long bones of the extremities, the patients affected with this disease show distinctive characteristics, such as disproportionally large head (usually of the brachycephalic type), relatively long trunk, depressed nose, trident hands, and dwarfed and curved extremities.

This condition has been recognized since the earliest recorded times. The artistic description of the gods of Bes and Ptha shows that the primitive Egyptians encountered this particular type of nanism. Although the disease was well recognized and its mental and physical shortcomings known, the separation of chondrodystrophy into a distinct type of deformity really dates from Parrot's description of the malady in 1878. Some years later, in 1892, Kaufmann, in a very interesting and extensive monograph, disclosed the essence of the disease.

Historical, histologic, pathologic, radiologic, and clinical treatises have been so numerous and so thorough that additional repetitions are not necessary. The purpose of this report is to present a case of achondroplasia in an adult, associated with pregnancy and labor, and to call attention to the peculiarities of this malady in relation to the sexual activities of adult women affected with the disease.

Chondrodystrophia in the adult is rare, and its association or coincidence with pregnancy and labor is still more infrequent. The textbooks of DeLee, Williams, Hirst, Dorland, Döderlein, Girol, Vignes, and Auvard make very little or no mention of the condition, and an extensive perusal of the literature at my command further confirms the conclusion. I believe that this is the first case reported from the island of Puerto Rico. The condition is unusual in the adult because very few achondroplastic children are born alive. Most of them die in utero or during delivery, and those born alive seldom reach maturity. Because of this high mortality it was believed that the disease was essentially fatal, but now we know that, although the prognosis is very grave in the severe cases, the lower gradations of the malady are not necessarily incompatible with life.

Porak, Kaufmann, Breus and others have showed that certain types of dwarfs in adults present chondrodystrophic modifications similar to those exhibited in the congenital cases. These patients have a very striking appearance. Their mental

faculties are usually normal. Sexual desire and sexual activities as a whole are comparatively normal. Their genital organs develop normally though Wagner has called attention to the fact that they are excessively developed. He found the uterus large and wide in some of his patients. The secondary sexual characteristics are manifest as a rule very early, usually at the age of ten years. Menstruation usually appears at the proper time, and its periodicity is normal. No abnormalities of the menopause have been reported. These women seem to reproduce easily. Rebattu has reported one case in which the patient was pregnant nine times. Abortions are not more frequent than in normal women. Pregnancy evolves normally until term in most cases. While pregnancy may be and usually is normal, the same cannot be said of labor because all of these women have pelvis narrow in all dimensions. In the average case the measurements are about two-thirds of the normal. Labor usually starts at term. The effacement evolves normally, but the dilatation is very slow and tedious, the membranes rupturing long before the dilatation is complete. Because of the serious dystocia character of these pelvis, delivery is impossible through the natural passages, and unless operative assistance is given, the patient becomes infected and dies. Porak, who has made an extensive study of this matter, was the first to give a full description of this particular type of pelvis. He has shown that there are two distinct types which can be distinguished definitely from the purely rachitic type, formerly placed in the same classification. In one, the main characteristic is the marked flatness of the superior strait, with a general contraction resulting in a reniform pelvis. The promontory in this type is high and prominent, and the sacrum, greatly inclined, lies in a nearly horizontal plane. The second type is very rare. Its chief distinction consists in a general contraction in the form of a triangle with the superior strait somewhat larger.

#### CASE REPORT

On the afternoon of June 25, 1934, a patient entered our maternity service, who because of her striking appearance, attracted the immediate attention of all the attendants. She was a twenty-year-old, fat, and extremely short woman at full term. Labor had started vaguely with weak, irregular pains, which came every two or three hours, lasting for about thirty seconds. Pelvimetry revealed a flat pelvis with a conjugate of 6.4 cm. An x-ray picture showed a flat, deformed pelvis with the fetal head unengaged because of great cephalopelvic disproportion. Urinalysis showed slight traces of albumin; the hemoglobin was 70 per cent (Dare), red cells, 4,140,000; and the coagulation time (Bogg), 2.5 minutes. A vaginal smear was negative for gonococci, and the Wassermann test was also negative. An immediate intraperitoneal hysterotomy was performed, delivering a male child who weighed 5 pounds 3 ounces. The baby was essentially normal.

#### CLINICAL HISTORY

The patient's father died two years previously in an accident. Her mother died ten years previously, cause unknown. Both the father and mother were normal individuals. The patient was the only child, but her mother had several abortions. Her past history was essentially negative. It revealed no trouble in walking or exercising. There was no history of trauma or osteopathologic heredity. She was married a year previously. Her husband, thirty years old, was tall and appeared normal. Menstruation began when she was fourteen years old; periodicity was normal, twenty-eight-day cycle, the flow was scanty, lasting three to four days with comenstrual pain for the first two days. She had never missed a period until this pregnancy, the last period occurring Sept. 13, 1933. The pregnancy had been uneventful in spite of the fact that she received no prenatal care.



The patient was forty-six inches tall. The head was of the brachycephalic type. The face had a squatty appearance and the nose was depressed. The trunk was practically normal, but the extremities were extremely shortened. The upper extremities reached only to the hip joints. The hands and feet were unusually small. The skin was coarse and dry. The deposition of fat was greater than average, especially in the abdominal and gluteal regions. The hair was normal in amount, appearance, and distribution. The finger nails were small and friable. The eyes, ears, nose, and throat were normal. Physiologic enlargement of the thyroid was present. The heart and lungs were essentially normal. The pulse was soft and regular, 90 per minute;



Fig. 1.—Photograph showing patient and baby beside a normal-sized woman.

blood pressure, 90/54. X-ray plates disclosed considerable lordosis of the spine, curving of the forearms, deformed wrist and knee joints and a small, flat, deformed pelvis with large obturator foramen, prominent sacrum, small flattened acetabula, and very short necks of the femurs. The muscles were well developed. The teeth were small but in good condition. The gums were normal. The abdomen was large, with a full-term pregnant uterus. The ovoid was longitudinal; the head was on the inlet, floating; the back was to the left and anterior; and the small parts were in the fundus. The fetal heart tones were audible 1 inch below and to the left of the umbilicus. External pelvimetry 18, 20, 21.5, 17. The vulva was small, and the vagina narrow with moderate discharge. The cervix was small, high, soft, and closed. The perineum was rigid and the outlet considerably contracted. The adnexa

and culdesac were normal. Vertex, L.O.A. The breasts were large and pendulous with erect and well-formed nipples.

The patient was of a highly nervous temperament; there were no pathologic reflexes. She was mentally competent, but her intelligence was below average.

#### COMMENT

This case presents the main clinical features and the most important radiologic characteristics of achondroplasia. It is remarkable inasmuch as it shows no secretory deficiency of the thyroid gland, no history of osteopathology, and no history of syphilis—three important causes which have been heralded by the majority of the students of this important subject in their interesting debates on the obscure etiology of this disease. The essential peculiarities of this condition in relation to the sexual activities, including pregnancy and labor, were not unusual. The patient was first seen when labor pains started. Her pregnancy had been uneventful, but labor was impossible through the natural passages because of the marked deformity and contraction of the pelvis. This constitutes the first case of this type reported in the island of Puerto Rico, where osteopathology and marked disturbances in growth are quite rare, possibly on account of the beneficial effects of the sunny climate.

#### REFERENCES

- (1) *Auvard*: Accouchement. (2) *Cebon, J.*: Contribution to the Study of Achondroplasia and Its Relation to Pregnancy and Delivery, Thesis, Paris, 1922. (3) *DeLee*: Principles and Practice of Obstetrics. (4) *Döderlein*: Tratado de Obstetricia. (5) *Dorland*: Modern Obstetrics. (6) *Halban, Seitz*: Biología y Patología de la Mujer 4: 523. Enciclopedia, 1932. (7) *Hirst*: A Textbook in Obstetrics. (8) *Girol*: Tratado de Obstetricia. (9) *Pajot*: Travaux D'Obstetrique. (10) Union Medicale, loc. cit., Litzmann 280, 1890. (11) *Porak*: De l'achondroplasie, cited by Halban, Seitz. (12) *Rebatu*: Cited by Cebon, Thesis, Paris, 1922. (13) *Smoke*: P. Am. J. Roentgenol. 29: 31, 1933. (14) *Vignes*: Fisiología Obstétrica, Normal y Patologica. (15) *Kaufmann*: Chondrodystrophia Fetalis, Berlin, 1892. (16) *Wagner*: Über Familiäre Chondrodystrophie Arch. f. Gynäk., 1913. (17) *Wheeldon, T. F.*: Am. J. Dis. Child. 19: 1, 1920. (18) *Williams*: Obstetrics.

## A TUBE FOR THE COLLECTION OF URINE UNDER ASEPTIC CONDITIONS

SOL LITT, M.D., CHICAGO, ILL.

(From the Department of Obstetrics, Michael Reese Hospital)

**O**FTEN it becomes desirable in gynecologic and especially in obstetric patients to collect a specimen of urine which will be free from contamination by vaginal discharges and lochia and which will avoid the necessity for catheterization with its attendant disadvantages. To this end the use of a simple device is recommended.

The collecting tube consists of an ordinary bent adapter, such as is used in chemical laboratories, the tube being 150 mm. long and bent at an obtuse angle. The wide mouth of the tube has an internal diameter of 18 mm. This type of tube is standard chemistry equipment, and may be purchased for a few cents at any chemical supply house. A few tubes may be kept sterilized and ready for use.

The tube is used to collect urine directly from the female urethra as follows: The patient is placed in a dorsal recumbent position in bed, the knees bent and

elevated as for vaginal examination. The labia majora are spread apart, and the region about the external urinary meatus cleansed with water and cotton pledgets avoiding the vagina and all parts except the area immediately surrounding the meatus. The mouth of the previously sterilized collecting tube is pressed gently around the meatus so that the external urinary orifice lies in the mouth of the tube. The patient is permitted to urinate, the urine passing directly into the tube and being collected in a receptacle placed below the small open end of the tube. The specimen is then removed for analysis.

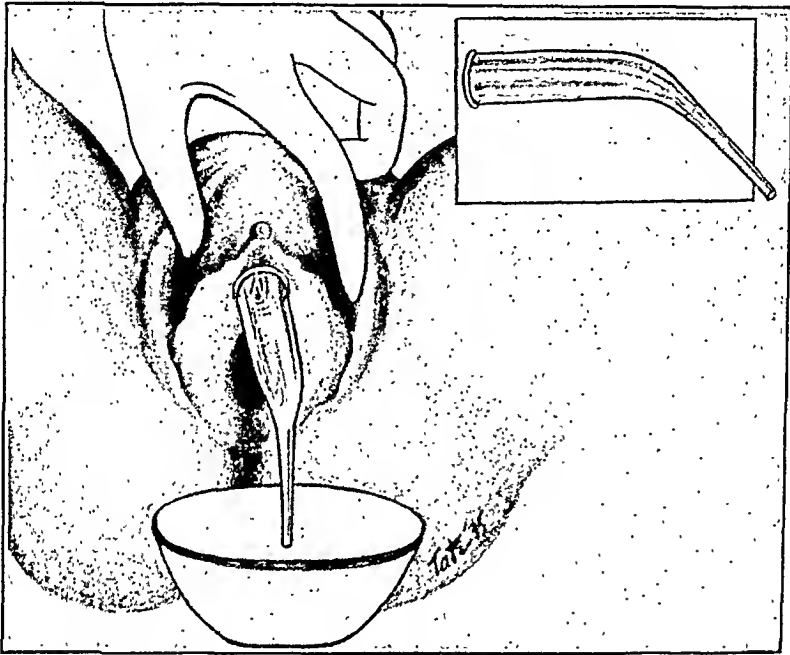


Fig. 1.—Collecting tube in place about external urinary meatus. Bent adapter used as collecting tube (insert).

Urine thus collected is received directly from the urethra into sterile containers, and all contamination from vestibule and vagina is eliminated. This is particularly advantageous in obstetric patients when a "clean" urine specimen is desired within a few days postpartum, since contamination by the lochia can be entirely avoided. Such specimens should show approximately the same findings as a catheterized specimen with the advantage of avoiding actual catheterization and its dangers.

185 NORTH WABASH AVENUE

## DIFFUSE SARCOMA OF THE ENDOMETRIUM

G. H. MOENCH, M.D., AND LOUISE H. MEEKER, M.D., NEW YORK, N. Y.

(From the Department of Gynecology and the Department of Pathology and Bacteriology, New York Post-Graduate Medical School and Hospital, Columbia University.)

SARCOMA of the myometrium is relatively infrequent since not more than 2 per cent of the fibromyomas of the uterus are true sarcomas. Even less common is sarcoma of the endometrium which occurs in a ratio of 1:6 to sarcomas arising in the myometrium (Meyer<sup>1</sup>). This ratio appears to us to be inordinately high as we were unable to find a record of a case of sarcoma of the endometrium in the files of the New York Post-Graduate Hospital. It thus seemed to us that a diffuse sarcoma of the endometrium was sufficiently unusual to be of especial interest.

The endometrial sarcomas are divided grossly into the more frequent circumscribed and the rarer diffuse types. The circumscribed is often polypoid and usually arises in the cervix in young individuals. The case we are reporting is an example of the diffuse type involving the entire endometrium. Sarcomas of the endometrium described by Meyer in Henke and Lubarsch cover the subject to 1930. Since then Ward<sup>2</sup> (1931), Needles<sup>3</sup> (1933), who included a sarcoma similar to the one reported here with three "polymorphous sarcomas," and Offergeld<sup>4</sup> (1933), have described diffuse endometrial sarcomas. The gross and histologic descriptions in these reports agree with our findings.

The history of our case was as follows:

J. B., white, married, female, fifty-five years old, with two children, twenty-seven and twenty-four years old, respectively, came to the dispensary of the New York Post-Graduate Hospital, April 3, 1933, complaining of frequency of urination for the past year and pain in the lower abdomen and profuse vaginal discharge for the past three months. There had been no loss of weight and no bleeding since the menopause, three years previous to admission.

Physical examination showed a rather stout patient with senile changes of the introitus and vagina, marked erosion of the cervix with profuse mucopurulent discharge. The uterus was retroverted, somewhat enlarged, and fairly hard. The cervix was coagulated with the Cherry bipolar electrode and healed very well but the discharge continued unabated. On May 15 a dilatation and curettage was performed by one of us (Moench) and a large amount of necrotic, friable, foul-smelling material mixed with pus and blood was evacuated from the uterus. The tentative diagnosis was necrotic fibromyoma or sarcoma, or carcinoma. A total hysterectomy was advised. This was done on May 26 (Moench). The cervix was first tightly packed with gauze soaked in iodine, the vagina thoroughly swabbed out with the same agent, and a laparotomy performed. Both adnexa were removed with the uterus. Because of the probability of malignancy no clamps were used on the uterus itself. The bladder was rather firmly attached to the uterus but was freed without mishap.

The patient did extremely well until the evening of the fourth day when she suddenly became cyanotic, with cold extremities, and was bathed in cold sweat. Pulse 110, respiration 30, temperature 101°. Despite all measures the patient died the next day. Although an autopsy was not permitted the cause of death evidently was of an embolic nature.

*Pathologic Specimen.*—The surgically removed specimen was a uterus (including the cervix and with both tubes and ovaries attached). It was 100 mm. in length and 35 by 40 mm. in diameter at the cervical end, and at the fundus measured approximately 42 by 35 mm. It had been split open disclosing a uterine canal lined by an irregularly thickened endometrium 20 mm. in thickness in some areas. The superficial portions were gray green in color, apparently largely necrotic and infiltrated by purulent exudate. In the deeper portion there was a gray opaque layer

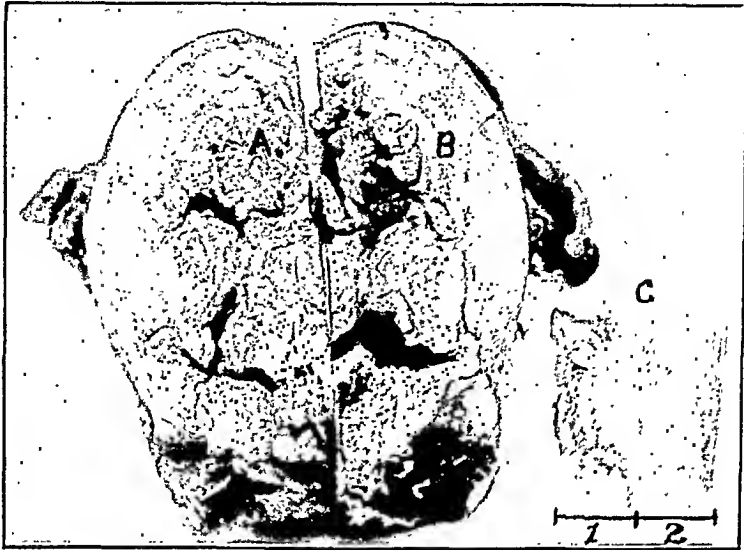


FIG. 1.—Uterus showing (A) diffuse, seminecrotic tumor roughly demarcated from (B) the myometrium. (C) Cross-section of uterine wall: (1) Diffuse thickening of endometrium (2) myometrium.



FIG. 2.—Cross-section of uterine wall (low power). A, Diffuse sarcoma of endometrium (no endometrial glands). B, Myometrium.

about 5 mm. in thickness which poorly demarcated the involved endometrium from the underlying myometrium. The serosal surface was smooth and the tubes and ovaries were without gross pathology. Besides the uterus itself (Fig. 1) there were also several pieces of partly necrotic grayish tissue apparently from the interior of the uterus, the largest measuring 35 by 25 by 22 mm. Sections extending through the ragged lining of the uterine canal and myometrium (Fig. 2) show the following microscopic pathology:

There is a lining of necrotic tissue and purulent exudate beneath which there is viable neoplastic tissue (Fig. 2, 4). The neoplastic tissue is formed by an edematous diffuse proliferation of somewhat irregular cells with large deep-staining nuclei and very abundant mitotic figures (Fig. 4). The cells which often form poorly defined irregular nests are in some places spindle-shaped and in other places present multiple branches which extend to the neighboring cells. When stained by van Gieson's or Mallory's connective tissue method, it is possible to recognize connective tissue fibrils running through and between these cells, indicating their origin from connec-

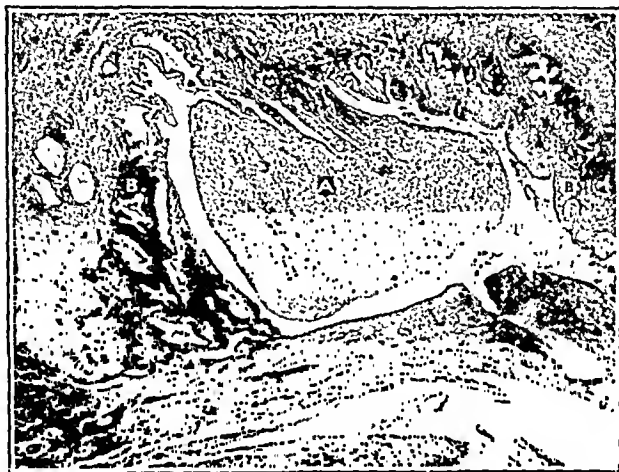


Fig. 3.—Section from cervical region (low power). A, Polyp of tumor projecting into dilated cervical gland. B, Cervical mucosa with normal glands.

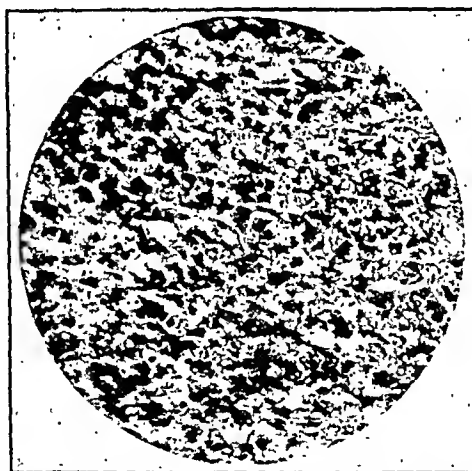


Fig. 4.—Endometrial growth (high power). Diffuse sarcoma cells of endometrium. Note relation to reticular fibers and the numerous mitoses.

tive tissue rather than from epithelium. There are no endometrial glands at any point and epithelial cells are not recognized. At the point of transition to the cervix the sarcomatous proliferation ends except for occasional extensions into the cervical gland ducts (Fig. 3). In some areas the neoplastic cells extend between the adjacent muscle bundles in the myometrium, and the deeper portions of the myometrium contain numerous collections of lymphocytes. *Diagnosis:* Diffuse sarcoma of the endometrium.

Meyer considers that all the variations of endometrial sarcoma are of one cell type derived from the endometrial stroma.

The diffuse sarcomas of the endometrium are usually divided into the following types: namely, those with (1) large round and spindle cells, (2) decidua-like cells, (3) giant cells with small round and spindle cells, and (4) small round cells (Ruge).

The manner of diffuse growth and the type of the neoplastic cells in our case warrant a diagnosis of diffuse round and spindle-cell sarcoma arising from the connective tissue of the endometrium.

#### REFERENCES

- (1) *Meyer, R.*: Das Schleimhautsarkom in Handbuch der speziellen pathologische Anatome und Histologie, edited by F. Henke and O. Lubarsch, Berlin, 1930, Julius Springer 7: pt. 1, p. 374. (2) *Ward, C. V.*: Canadian M. A. J. 25: 707, 1931. (3) *Needles, R. J.*: Am. J. Cancer 19: 364, 1933. (4) *Offergeld, H.*: Ztschr. f. Krebsforsch. 39: 191, 1933. (5) *Ruge (cited by Ewing)*: Winter, G.: Lehrbuch der gynäkologischen Diagnose, Leipzig, 1907.

---

Superbi, Carlo: Echinococcic Cyst of the Liver During Pregnancy, Clin. ostet. p. 639, 1935.

The author describes a case of suppurative echinococcus cyst of the liver which was mistaken for an ovarian cyst and discusses the symptomatology of pregnancy complicated by echinococcus cyst. After eleven hours of labor of this primigravida, a midwife discovered the presence of a complicating abdominal tumor. The author, immediately summoned, excluded twin pregnancy and ascertained a cystic tumor apart from the pregnant uterus. The patient was spontaneously delivered of a live child. She reacted normally, had no rise of temperature during the puerperium and entered the hospital forty days postpartum for removal of the cyst. At that time the abdominal mass, smooth surfaced and movable, slightly deviated to the right, reached three fingers above the umbilicus. Normal sized uterus, anteverted, movable, was palpated to be not connected with the mass. At laparotomy tumor was found to be attached to right lobe of liver with dense adhesions to liver, gallbladder and omentum and was removed with difficulty. Abdomen was closed with opening left for drains. With rise of temperature on seventh day pleuritic exudate developed. Purulent fluid was removed twice, 150 and 170 c.c., respectively. Finally rib resection was done resulting in perfect recovery. A few months later patient again became pregnant and later gave birth to a full-term baby.

The removed cyst weighed 3,600 gm. and consisted of two parts, the one the size of an orange, the other the size of a seven months' pregnant uterus. They contained a purulent, yellowish fluid with many echinococcal cysts.

Failure of proper diagnosis is excusable in the face of the assertion of many writers (Mangiagalli, Boursier, Abadie and others) that differential diagnosis between echinococcal and ovarian cysts is difficult. Franta (1902) collected from the literature 51 cases in which the first symptoms of echinococcus appeared during pregnancy, and 40 instances in which they were discovered during the puerperium. Some writers (Alfieri, Bertino and Alamanni) recorded their rapid growth during pregnancy. In the opinion of Franta, pregnancy favors not only growth but also suppuration of these cysts. As shown in Superbi's own case, the complicating echinococcal cyst may not interfere with pregnancy, labor or development of the fetus. When located in the pelvis, the cyst may cause abortion and more often becomes responsible for dystocia endangering the life of the fetus.

AUGUST F. DARO.

# Department of Maternal Welfare

---

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

---

## THE EVALUATION OF PRENATAL CARE\*

IN VIEW of the increasing interest in maternal morbidity and mortality and the emphasis placed on prenatal care by physicians and administrative groups in general and obstetricians in particular, the recent report by Drs. Tyler, Watkins, and Walker is particularly significant. Their study is an attempt to evaluate quantity and quality of prenatal care. The specific question for which the answer was sought is stated thus: "If all other contingent factors are the same, what, if any, is the effect on the survival of the mother of various services described as prenatal care?"

Under careful supervision the records of 285 ward deliveries taking place in the New Haven Hospital, and 930 ward and out-patient delivery records of the Boston Lying-In Hospital were subjected to very careful scrutiny and statistical juggling.

Elaborate four-page record forms for compilation of data were used. From data so obtained patients were grouped accordingly as they received adequate or inadequate prenatal care. It is pointed out that the term "inadequate care" rather than "no care" was used because so few patients can be found among deliveries of a high grade maternity service who have had no prenatal care.

After careful grouping according to quantitative standards of prenatal care received, the groups thus resulting were balanced with reference to age, parity, plurality, legitimacy, color, race, economic status, and time of year. Comparison was thus secured at the expense of decided diminution in group numbers, serious but perhaps unavoidable objection to the study.

The balanced groups thus obtained were then subjected to searching analysis of complications of pregnancy and labor and the outcome of delivery. "The groups were found to be strongly influenced in the first outcome by a lack of balance revealed in complications of pregnancy. Apparently, women who have knowledge of some previous impending complication bestir themselves to obtain considerable care and attention. Conversely, those who have gone through former pregnancies without difficulty, or have otherwise found no reason for fear, appear often to neglect proper prenatal care, and will accordingly be classed in the B or intermediate group." (A, adequate prenatal care. B, inadequate and C, intermediate.) "To adjust for this a final balancing of the A and B groups with respect to complications of pregnancy was carried out with the large Boston case series. The excess of each complication (in one group or the other) was removed through random withdrawal by lot from all those who had that particular complication. A final recheck of age, parity and the like was then made to insure that balance of those factors had not been unduly disturbed. The end result was the formation of two comparable groups (A and B) differing only in the degree of prenatal care received, in which groups the course of labor and the final outcome could be studied."

---

\*Report on the Evaluation of Prenatal Care, by Drs. Tyler, Watkins and Walker, Yale University School of Medicine. Published by the Institute of Human Relations, New Haven, Conn., 1934.



The report is interesting, timely and significant. It is well written and apparently fulfills necessary statistical requirements. From data obtained the authors draw certain conclusions, most significant of which is their failure to demonstrate benefits of prenatal care. While the conclusions drawn are doubtless tenable on the basis of data studied, I cannot believe it correctly evaluates prenatal care. In the first place, the study is a comparison of groups receiving prenatal care and frequency or number of prenatal visits is not always a safe index to its quality. Second, whether the number of records studied is adequate may be seriously questioned. The benefits accruing to patients from prenatal care can be ascertained only by comparing with large groups not so fortunately cared for. Furthermore, many complications of pregnancy are uncommon and no satisfactory evaluation of prenatal care in these cases can be hoped for except through analysis of very large groups. It is unfortunate that the basis for comparison in the series studied was not more satisfactory. The doubt and misunderstanding engendered by this report may delay but will not prevent a healthy development of prenatal care.

That prenatal care fails to accomplish a marked reduction in the number of complications at the time of delivery, is not surprising. In general with the exception of deformities, toxemias, and complications arising from coexisting disease (tuberculosis, nephritis, heart disease, etc.), most delivery complications cannot be foreseen. Recognition of abnormalities during pregnancy does not necessarily minimize the problems to be faced at the time of delivery. Knowledge of these threatening potentialities is nevertheless worth while even though we cannot always use it to advantage—an indication, perhaps, of shortcomings in the management of labor rather than futility of prenatal care. Such complications as placenta previa and premature separation are not prevented by prenatal care, but such care is likely to render patients more awake to untoward symptoms and therefore lead to earlier application of remedial measures.

If prenatal visits do no more than give the patient confidence and moral support during pregnancy such care still would be worth the effort. It does much more than this, however, for as pointed out in the preface to this report, “. . . experience of hospital and home delivery maternity services in England and in this country is quite uniform to the effect that maternal mortality, the incidence of stillbirths, and the neonatal mortality are lower when the expectant mother has had appropriate prenatal supervision, at least during the last three months of pregnancy, than is the case when women of similar parity, age, race, and economic status; and with comparable obstetric and aftercare, are delivered without having had the benefit of the medical and nursing supervision. In such conditions as syphilis in the expectant mother and in women with contracted or deformed pelvis, the value of prenatal medical examination is so great as to be beyond dispute.” The many intangible benefits which accrue to patients from adequate prenatal care are probably not accessible for statistical measurement. Prenatal care has not been overemphasized, but there is abundant evidence to show that care at the time of delivery and thereafter has been greatly underemphasized.

A pertinent point brought out in this study is that: “Negative prenatal care benefits throughout our several projects have been interpreted as substantiating the growing feeling that obstetric care at labor may play by far the greatest rôle in improvement of maternity outcome. If this be true, prenatal care can render a signal service by directing pregnant women to make arrangements for a high quality delivery service.”

No amount of prenatal care can compensate for poor care at the time of delivery, but good care at the time of delivery can often compensate for lack of prenatal care and can be the most potent single factor for good or bad obstetrics.

—Norman F. Miller, M.D.

# Department of Book Reviews

---

CONDUCTED BY ROBERT T. FRANK

---

## Review of New Books

### Endocrinology

The second edition of *Recent Advances in Endocrinology*<sup>1</sup> by Cameron differs from most of the books on the subject, in that it stresses the fact that endocrinology is "essentially a biochemical subject." Written by a biochemist, on the very first page of the introduction the author emphasizes a statement, the truth of which I have for many years tried in vain to sell to the profession, namely, that a given gland may produce "too much or too little of these specific compounds but it does not produce abnormal compounds."

This book, from cover to cover, is replete with accurate information, particular emphasis being laid upon the biochemic phases of endocrinology. It is surprising that a biochemist has been able to summarize the clinical aspects with such clearness and decisiveness. Occasionally while trenching upon therapy he has been slightly misled but not to anything like the same degree noted in most books on this subject.

The literary references are also extremely well chosen and cover the subject up to August, 1934.

All in all this is a most exceptional and valuable book which can be studied with equal profit by the practitioner, the specialist, and the experimentalist in this subject.

—R. T. Frank

The second edition of *Hormone und Innere Sekretion*<sup>2</sup> appears six and a half years after the first. Some six thousand new publications have been incorporated, which has almost doubled the size of the book. This is the summary of endocrinology covering general endocrinology, pancreas, thyroid, parathyroid, adrenal, hypophysis, the gonads, as well as other glands without external ducts which have been considered as possible sources of internal secretions. To some extent it resembles our physiologic reviews, except that the entire field has been covered in 368 pages. As most of the references have been taken from abstracts, a large number of minor errors have crept in which, however, are largely compensated for by the fact that the author has a wide and deep acquaintance with endocrinology.

This epitome will be found of great use in locating references or rapidly surveying the field of endocrinology, as it is well arranged and each chapter is followed by a fairly full bibliography.

—R. T. Frank

---

<sup>1</sup>*Recent Advances in Endocrinology*. By A. T. Cameron, Ed. 2, with 55 figures, including 2 plates, and 406 pages. P. Blakiston's Son & Co., Philadelphia, 1935.

<sup>2</sup>*Hormone und Innere Sekretion*. Von Dr. Fritz Laqueur, Professor an der Universität Frankfurt. Zweite, verbesserte und bedeutend erweiterte Auflage. Verlag von Theodor Steinkopff. Dresden, 1934.

Harrow and Sherwin have attempted the difficult task of making the *Chemistry of the Hormones*<sup>3</sup> accessible to the medical profession. The text is so well arranged and so simplified, as well as supplied with chemical formulas, that even the physician who has not kept up with modern organic chemistry can obtain much knowledge from its pages. The authors have taken up the various hormones, some of which, like the thyroid, the adrenal medullary, the male and female sex hormones, have been isolated. Such properties as are known of the less well isolated hormones are likewise described. It contains an enormous fund of information. As the advances in this field are so rapid, it will require frequent revision. For example, since its publication in April, 1934, the chemical and structural formula of progestin as well as its synthesis from the soya bean have been developed, which, of course, could not be incorporated in this valuable monograph.

—R. T. Frank

Goldzieher's *Practical Endocrinology*<sup>4</sup> is designed as a guide to the general practitioner, particularly to help him interpret symptoms and to "direct his attention to the culprit gland." In its preface the author emphasizes that he is largely influenced by the pioneer work of Allen Winter Rowe.

The introductory chapters on the morphology and physiology of the glands are purposely short and clear. The chapter on examination of the endocrine patient gives an excellent résumé of the various biologic and pharmacologic tests which will be found useful to the general practitioner for understanding the rationale and purpose of these tests. The description of the symptomatology, on the whole, bears careful scrutiny.

The same cannot be said for the therapy, which, on the whole, is much more optimistic than the reviewer feels warranted, as he does not have the same confidence in diagnosis or the efficacy of the drugs and products recommended. This book compares favorably with a large number of similar volumes which are appearing at the present time. Its chief merit lies in the fact that the author has a wide experience in endocrinology which he has presented in an understandable fashion.

—R. T. Frank

Another approach to the study of cancer is offered in da Costa's monograph *The Action of Hypoglycemic Substances Upon Certain Fermentative Processes of Neoplastic Tissue*<sup>5</sup> which forms one issue of the "Arquivo de Patologia," published by the Portuguese Institute for the Study of Cancer. The author has studied both normal and neoplastic tissues in both human beings and animals from the chemical, pharmacologic, and therapeutic points of view. He has devoted himself mainly to the effects produced by insulin and allied substances upon those having neoplasms. He finds that insulin injected into animals having neoplasms produces a diminution in the size of the tumors, but not their complete regression; that all tissues, both neoplastic and normal, show a hypoglycemic substance, an "insulinoid," more abundant in the former than the latter; that hyperadrenalinemia and hyperglycemia are produced in animals and in human beings by radiotherapy, and that insulin applied locally to tumor tissue results in a cicatrization and regression of the tumor.

<sup>3</sup>The Chemistry of the Hormones. By Benjamin Harrow, Ph.D., Associate Professor of Chemistry, City College of New York, and Carl P. Sherwin, M.D., of St. Vincent's and French Hospitals. Williams and Wilkins Company, Baltimore, 1934.

<sup>4</sup>Practical Endocrinology. By Dr. Max A. Goldzieher, Endocrinologist, Gouverneur Hospital, etc. Illustrated, 326 pages. D. Appleton-Century Co. Inc., New York, 1935.

<sup>5</sup>Arquivo de Patologia. Orgao do Instituto Portuguez Para O Estudo do Cancro. Publicado por F. Gentil e M. Athias. Vol. VI, No. 2, Agosto, 1934. Palhava, Lisboa.

There are also numerous studies on the effects of radiotherapy and the action of insulin upon the tissues so treated.

The work is painstaking and thorough, and the literature has been completely covered. It should prove invaluable to those working along cancer lines.

—Frank Spielman

## Obstetrics

In these days of frequent cesarean sections it is refreshing to find a book on operative obstetrics which stresses delivery from below. DeCamargo's *Manobras e Operacoes Obstetricas*,<sup>6</sup> with a foreword by Magalhaes, is to be praised if only for this reason. The different maneuvers which can be utilized in vaginal delivery are clearly, concisely, and intelligently presented. It is astounding to ponder upon the enormous number of methods in use. Nor is abdominal cesarean section neglected. The work, however, is an excellent testimonial to the fact that operative obstetrics can be taught and learned, but that obstetrics must remain an art in which the judgment of the individual in the choice of maneuver or operation is of prime importance.

It may be suggested to the author that his extensive bibliography, evidence of considerable effort, can stand revising. Many inaccuracies as well as mistakes in spelling are found here. His illustrations although adequate may also be improved. On the whole, in the field of operative obstetrics the book covers the ground thoroughly.

—Frank Spielman

Short concise texts in medicine may be exceedingly useful. The average monograph, whether published in book form or as a long article, serves as an example. Of course, in this type of work the author almost invariably limits himself to one particular phase of a subject and usually treats it exhaustively. On the other hand, attempts are repeatedly being made to boil down entire medical specialties within the covers of books two or three hundred pages long. The following two books, little more than pamphlets, fall within this category, and are therefore reviewed together.

Devraigne, as part of a "medical introduction" series, contributes two short books on obstetrics, viz. *Propédeutique Obstétricale*,<sup>7</sup> and *La Pratique Obstétricale*.<sup>7</sup> The former consists of seven short chapters dealing with fecundation, development of the fetus, examination of the patient, normal delivery, and the normal presentations. The latter discusses briefly infectious diseases, toxemias, gastrointestinal conditions, blood and urinary abnormalities, and affections of the nervous system associated with pregnancy. There are also uterine anomalies, abnormalities of the uterine muscle, of the soft parts, and of the pelvic girdle. Operative obstetrics is covered in very few pages. Taken together, these two books give the impression of disconnected, disjointed material hastily got together for publication. They are neither fish nor fowl nor good old-fashioned obstetrical primers.

—Frank Spielman

<sup>6</sup>*Manobras e Operacoes Obstetricas*, pelo Docente Dr. Joao Pereira de Camargo. Livro Docente da Faculdade de Medicina da Universidade do Rio de Janeiro, etc. Segunda edicao correcta e augmentada, contendo 15 trichromias, 242 clichés e 4 microphotographias. 498 pages. Livraria Francisco Alves, Rio de Janeiro, 1935.

<sup>7</sup>*Propédeutique Obstétricale*. Par L. Devraigne, accoucheur de Lariboisière. 191 pages. Masson et Cie, éditeurs. Paris, 1934.

*La Pratique Obstétricale*. Par L. Devraigne, accoucheur de Lariboisière. 244 pages. Masson et Cie, éditeurs, Paris, 1935.

This little volume, entitled *Aid to Obstetrics*,<sup>8</sup> as a matter of fact is designed as an aid to students preparing for an examination in obstetrics. For this purpose it is well adapted, since it brings in succinct form all essential facts, including indications and details of technic of most obstetric operations. Its appearance in a tenth edition must be accepted as proof for its usefulness and popularity.

—Hugo Ehrenfest

Among the diseases encountered as complications of pregnancy, *Pulmonary Tuberculosis*<sup>9</sup> holds first place both in regard to frequency and practical importance. Though an enormous literature has accumulated, the question of the effects of disease and pregnancy on each other has remained unsolved. In marked distinction to many previous contributions in this monograph the exact histories are presented of 360 pregnancies observed in 215 tuberculous women. Diagrammatic sketches, x-ray plates and graphic charts establish for almost every case not only actual conditions but as well the changes noted in the course of many years. Critical analysis of the case records and appropriate tabulations from various viewpoints permit clear insight into the life histories of all these patients. From them the author draws his conclusions which start with the significant statement: "The problem of pregnancy in the tuberculous woman is not solved." In his opinion, it is possible to determine with some certainty for some patients the probability of acute and even dangerous aggravation of her disease, but this unfortunate effect certainly is rarer than commonly believed. There are means available to protect the woman against such a deleterious effect. No definite rules can be established for advisability or necessity of interruption of pregnancy.

Though the writer's views, especially in regard to contraception, sterilization and even interruption, are clearly and inevitably influenced by laws and public opinion at present prevailing in Germany, the monograph proves of unusual interest and value particularly through its careful presentation and critical analysis of the large material.

—Hugo Ehrenfest

This small monograph<sup>10</sup> deals with the *Unexpected, Sudden Death of the Patient During Pregnancy, Labor, and Puerperium*. It consists of a thorough review of all reported cases in which sudden death was due chiefly to a great variety of complicating and often unsuspected diseases and anomalies.

—Hugo Ehrenfest

This historical volume<sup>11</sup> includes 15 communications of various authors, dating from 1770 to 1831, on the subject of *Symphysiotomy*.

It is gotten up in a faultless fashion with a number of portraits and illustrations. The material was collected and edited by *Nederlandseh Tijdschrift voor Geneeskunde*. It should prove of great interest to those interested in the history of medicine, particularly those who read the Dutch language.

—R. T. Frank

<sup>8</sup>*Aids to Obstetrics*. By Leslie Williams, Obstetric Surgeon to Out-Patients, St. Mary Hospital, London, etc. Tenth edition. William Wood & Co., Baltimore, 1934.

<sup>9</sup>*Lungentuberkulose und Schwangerschaft*. Von H. Braeuning, Chefarzt der Fues-sorgenstelle fuer Lungenkranke in Stettin, etc. 275 pages. Mit 391 Kurven und Abbildungen. Verlag von Georg Thieme, Leipzig, 1935.

<sup>10</sup>*Der Unvermutet Schnelle Tod in Schwangerschaft, Geburt und Wochenbett*. Von Geh. Med. Rat Professor Dr. Erwin Kehler, Direktor der Univ. Frauenklinik in Marburg. 52 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

<sup>11</sup>*Opuscula Selecta Neerlandicorum de Arte Medica. Varii auctores de symphysiotomia*. Aangeboden door het Nederlandsch Tijdschrift voor Geneeskunde, 1934.

This report on the *Evaluation of Prenatal Care*<sup>12</sup> is the subject of a special communication by Prof. Norman Miller in this issue of the JOURNAL.

—R. T. Frank

This monograph, on *The Conception Period of Women*,<sup>13</sup> translated from the Japanese and published in the United States, gives a summary of Ogino's views. His personal observations are based on 132 laparotomies in which the time of the menstrual cycle was compared with the ovarian findings. He also has a moderate number of personal observations on the time of conception and the time of so-called functional sterility in the cycle.

Ogino reviews both the provoked ovulation theory as well as the effect of cyclical trauma. In regard to the latter he has convincing evidence obtained after the earthquake of 1923. In the month succeeding the catastrophe, he obtained the menstrual cycles of over 200 high school pupils in the affected area and compared it with a similar group in an area not involved, without finding any change.

According to Ogino, the sterility phase begins twenty-four hours after ovulation. Sperma, he claims, is at most able to fertilize for three days.

This brief monograph is of great interest as it summarizes the world's literature in an excellent fashion and gives a clear-cut outline of the author's personal views. However, I feel that the material is far too scant as yet to permit us to consider the Ogino-Knaus hypothesis definitely proved.

—R. T. Frank

This report on *Maternal Mortality in Philadelphia*<sup>14</sup> contains a wealth of statistical material which appears to have been carefully collected and thoroughly and impartially digested. The problem of maternal deaths in Philadelphia, according to the committee, is fourfold, namely (1) self-induced and criminal abortions; (2) errors in judgment on the part of the medical profession; (3) lack of appreciation of the need of prenatal care by the laity; (4) failure of hospitals, organized medicine and allied agencies to grasp fully their responsibilities and opportunities.

The committee finds that the largest proportion of deaths from criminal abortion is among married women, many of whom having living children. The committee, although not unanimous, appears to favor the advisability of legalization of abortion with proper reservations. In Philadelphia the midwife is almost a negligible factor in connection with mortality, particularly as she is so closely supervised and her activities regulated. The laity is responsible in many cases through ignorance and lack of cooperation in causing preventable deaths. The report appears to be direct, straightforward, and with every effort to favor improvement in order to safeguard the obstetric patient.

—R. T. Frank

The *Elements of Experimental Embryology*<sup>15</sup> deals with the embryology of the prefunctional period mainly. It contains an amazing and bewildering mass of facts and ingenuity of experimentation by means of which some of the basic life processes

<sup>12</sup>Report on the *Evaluation of Prenatal Care*. By Margaret Tyler, J. H. Watkins, and H. H. Walker. A Report to the Sub-Committee on Evaluation of the Committee on Administrative Practice, American Public Health Association. 68 pages. Institute of Human Relations, Yale University, 1934.

<sup>13</sup>Conception Period of Women. By Dr. Kyusaku Ogino. English Translation by Dr. Yonez Miyagawa. Medical Arts Publishing Co., Harrisburg, Pa., 1934.

<sup>14</sup>Maternal Mortality in Philadelphia, 1931 to 1933. Report of the Committee on Maternal Welfare, Philip F. Williams, M.D., Chairman, Philadelphia County Medical Society, 1934.

<sup>15</sup>Elements of Experimental Embryology. By Julian S. Huxley and G. R. de Beer. With 221 illustrations and 514 pages. Cambridge University Press—Macmillan Co., New York, 1934.

have been analyzed. In differentiation it is immaterial whether a given nucleus finds a given cell. Up to a certain stage in gastrulation the fates of most regions are not irrevocably determined, as shown by transplantation experiments, except in the case of the chorda mesoderm.

Polarity and bilateral symmetry, however, are fixed. The axis of polarity is determined outside of the egg by such influences as light and chemicals. The plane of bilateral symmetry in the frog, for example, is determined by the point of entry of the sperm. All vertebrates are in reality asymmetrical.

Cleavage has little importance in differentiation. The egg of a fly, for example, cleaves only when the multiple nuclei finally reach the periphery. Until then, the cytoplasm is undivided. The dorsal lip of the gastropore in the lower forms acts as an organizer, a formative stimulus which brings about determination of the tissues. Its effect basically must result from chemical influences as the organizer tissue acts when dead and extracts of the organizer tissue likewise act. The composition is probably lipoidal.

Of great interest to the gynecologist and obstetrician is the section devoted to the gonads and sex differentiation. None of the evidence presented settles finally the controversy as to whether the primordial germ cells arise in the special gonad-field or come from elsewhere in the ovum. The authors consider the evidence conclusive that the indifferent gonad-rudiment is normally dependent on its genetic sex constitution although this can readily be overridden by other agencies. The gonad-field has one of two potentialities according to the sex chromosomes which it contains. The primordial germ cells appear to be completely bipotential as regards sex. The final determination depends on local influences. In the cortex they become female; in the medulla, male. Locally, temperature likewise plays a big rôle.

A considerable portion of the book is devoted to fields and gradients. The appendix is devoted mainly to a new type of experimentation devised by Holtfreter, based on the discovery that removing the membranes from the early blastulae of axolotls and then placing the tissues in Ringer's solution causes eversion of the layers or so-called exogastrulation and separation of the ectoderm with all of its resultant nervous tissue from the endomesoderm.

This book will prove most fascinating to any reader who is interested in the fundamental problems of biology.

—R. T. Frank

*Introduzione allo Studio Dell' Eugènica*,<sup>16</sup> by Cristalli, is obviously designed for the novice as an approach to the study of eugenics. The commonly accepted views are presented with adequate illustrations and ample references to the literature. Appended is a glossary of terms peculiar to this field. The material is elementary.

—Frank Spielman

Dr. J. Morris Slemons has written *A Handbook for Women During Pregnancy*.<sup>17</sup> It begins with the signs of pregnancy and the date of confinement, and covers embryology, prenatal care, labor, puerperium, and the lactation period. Written by an experienced obstetrician, it doubtless will find its field and circle of readers.

—R. T. Frank

<sup>16</sup>*Introduzione allo Studio Dell' Eugènica (Eredità biologica)*. Par Prof. Giuseppe Cristalli. Stabilimento Industriale Editoriale Meridionale, Napoli, 1934.

<sup>17</sup>*The Prospective Mother. A handbook for women during pregnancy*. By J. Morris Slemons, M.D. Third edition. D. Appleton-Century Co., Inc., New York, 1931.

It is interesting to note that essential instruction can be provided for expectant mothers and prospective fathers also in a (more or less) humorous form. *The Stork Joins the Blue Eagle*<sup>18</sup> is an amusing little volume, in spots (e.g., the chapter entitled: Obstetrical Ward), really funny. As a whole, the author presents only facts which are generally accepted, and recognized as important for up-to-date obstetric care, though we do, incidentally, not share his belief in the practical value of a urinary test for the purpose of determining the sex of the fetus. The Pipe Dream, in the last chapter, picturing the future work of the obstetrician under an NRA code, was interrupted a bit too early by that ringing phone. We had expected that such a code would as well decree a definite shortening of the hours of labor. A provision of that sort, unlike any other existing code, would be heartily approved by both the employer and employee. (This review was written before the Supreme Court decision.)

Every obstetrician should try to keep this little book in his waiting room and, since this probably will not be possible, might preferably induce every pregnant patient to acquire a copy.

—Hugo Ehrenfest

Dr. Kenyon's book on *Healthy Babies*<sup>19</sup> is designed for the expectant mother or the mother of a young child. She therefore devotes chapters to prenatal care and the baby at birth, as well as carrying the child through the third year of infancy. I am sure that many mothers will turn to its pages for help and doubtless and as usual, will here and there be misled when they try to be the child's own physician.

—R. T. Frank

*Diseases of Children*,<sup>20</sup> the standard of its kind in England for a number of years, is now in its third edition. New chapters have been added on blood transfusion, heredity, orthodontia, the newly born infant, diseases of the accessory nasal sinuses and ear, the lipoidoses, acetoneuria, cystoscopy and pyelography, rheumatism, allergy, and tuberculosis. Despite the rather formidable number of authors whose names appear on the title page, this by no means completes the list, other writers, thirty-six in all, contributing special articles throughout the work. Naturally, some of these will appeal to the reader more than others, but the treatment of the subject matter is so different from what we are accustomed to in this country, that there are very few chapters which will not have a definite appeal to the American reader. The chapters on functional and organic diseases of the nervous system, diseases of the muscles, and rheumatism were especially fascinating to this reviewer. Happily, the gap which has long existed between the English and American views on the nutritional disorders has been very much narrowed in this edition of the work, a fact which adds to its value as a reference work in this country. In fine, it would seem that no pediatrician who wishes to keep up with the advancement of pediatric thought can afford to be without this book, and even the physician whose interest in the diseases of childhood is a more casual one will soon find that the money spent for this volume is one of the best investments in his medical library.

—T. C. Hempelmann

<sup>18</sup>*The Stork Joins the Blue Eagle*. By Fred'k M. Margaretten, M.D. Illustrations by George S. Jacobs. Wamba Printery, Brooklyn, N. Y., 1934.

<sup>19</sup>*Healthy Babies and Happy Babies*. By Josephine Hemenway Kenyon, M.D. Little, Brown, and Company, Boston, 1934.

<sup>20</sup>*Diseases of Children*. Third edition with contributions of thirty-six authors edited by Hugh Thursfield, physician, Hospital for Sick Children, etc. and Donald Paterson, Physician to Out-Patients, Hospital for Sick Children, etc. William Wood and Company, Baltimore, 1934.



Zahorsky's *Synopsis of Pediatrics*,<sup>21</sup> as the title frankly states, is really a "synopsis." The author emphasizes that he "has tried to cover the essential points in symptomatology, diagnosis, and treatment," and in this he has succeeded admirably. As is to be expected the print is small, the illustrations are few, and the subject matter is treated in short paragraphs composed of short sentences. One experiences a feeling of haste while reading it.

—Frank Spielman

## Gynecology

The second half of the sixth volume of Stoeckel's *Handbuch der Gynäkologie*<sup>22</sup> is devoted to the clinic of uterine tumors. This is a huge contribution, 838 pages in length and costing 148 R.M.

It is somewhat unequally divided but covers a tremendous ground. The late v. Peham deals with the etiology, symptomatology, and treatment of uterine myomata in 181 pages.

P. Esch described uterine sarcomata in 31 pages. H. Martius covers radiotherapy of uterine myomata and sarcomata in 185 pages. O. Pankow devotes 400 pages to the therapy of uterine carcinoma and chorionepithelioma, including a shorter contribution of Schönholz on chemotherapy of cancer.

Peham in his description of myomata, contributes nothing new to the etiology. In 1,878 fibroids, carcinoma was found in 3.8 per cent (corporeal 0.53 per cent, cervical 3.3 per cent). He found no excess of corporeal carcinoma. Sarcoma was noted in only 2.78 per cent. He believes that the symptoms following castration are greater than those following hysterectomy.

Esch finds that there is 1 sarcoma to 28 carcinomata of the uterus. In 2,914 cases of uterine neoplasia, 1.3 per cent was sarcoma.

Martius believes that the roentgen effect on myomata is purely through the ovaries. He believes that treatment can be graduated so as not to destroy completely the ovarian function, but merely to bring about an "exorulation." He likewise considers the symptoms following hysterectomy less marked than following x-ray treatment. He found no increase of carcinoma after radiotherapy of myomata. He is strongly opposed to temporary sterilization as he believes that it has a bad effect on subsequent pregnancies, nor is he in favor of preputiary and splenic radiation. He likewise deals with the radiotherapy of sarcomata. The effect of radium in the uterus he considers more upon the mucosa but likewise affecting the ovaries. His descriptions of technic are sufficiently detailed to interest the radiotherapist, but likewise understandable to the gynecologist who has not equipped himself especially in this branch.

Pankow describes in utmost detail the operations for uterine carcinoma both from above and below. Likewise the radiotherapeutic treatments and combinations of operation and radiotherapy. The statistics and literature dealing with operability and mortality, and final results are given in great detail. He believes that the preference as to operation or radiation and operation is by no means settled. In the treatment of corpus carcinoma he advises to start the operation abdominally in order to remove the glands and then, depending upon individual preference, experience or the type of case encountered, to finish by a complete hysterectomy either through the abdomen or by the vaginal route.

<sup>21</sup>*Synopsis of Pediatrics*. By Dr. John Zahorsky, professor of pediatrics, St. Louis University Medical School, etc. With 77 illustrations in the text and 6 color plates. 349 pages. The C. V. Mosby Co., St. Louis, 1931.

<sup>22</sup>*Stoeckel's Handbuch der Gynäkologie*. Sechster Band, zweite Hälfte. Die Klinik der uterinen Tumoren bearbeitet von Esch, Martius, Pankow, Peham und Schönholz. Mit 169 zum Teil farbigen Abbildungen im Text. 835 pages. Verlag von J. F. Bergmann, München, 1931.

Schönholz's chapter on chemotherapy gives a very excellent review of the literature. The author concludes that at present we are not yet justified to treat carcinoma solely by chemical means.

The 160 illustrations in the text are mainly from standard sources such as Peham-Amreich: *Gyneecological Operations*; Sehaute, Stoeckel, Wertheim, Franz, etc.

This volume is of particular value to the clinician as it enables him to find the references to original sources collected in a conscientious fashion.

—R. T. Frank

Meigs's *Tumors of the Female Pelvic Organs*<sup>23</sup> is largely a personal book and is in the main based on a series of cases which the author studied from the Massachusetts General Hospital. Its appeal should be mainly to the general surgeon who does gyneecologic work, although the gyneecologist, pathologist, and roentgenologist may find matters of interest within its pages.

More than one-fifth of the book is devoted to carcinoma of the cervix. In 45,503 admissions to the Massachusetts General Hospital, among married patients, over thirty years of age, 1.6 per cent showed carcinoma of the cervix. The author appears a disciple of the chronic irritation theory as the causation for cervical cancer. However, he emphasizes that repair of lacerations, as shown by Woolston's series, did not reduce the incidence of the disease. He recognizes that biopsy material produces many inaccuracies of grading, but believes that examination of the entire uterus with grading in mind, is of value. Of the 110 cases at the Massachusetts General Hospital, one-half of the patients were operated upon and one-half were treated by radiation. In the 13 cases of stump carcinoma, Meigs considers the prognosis poor. This is contrary to my personal observations.

In many of the conditions the series of cases are too small to make the statistics of value. In fibroids of the uterus, 44 cases or 0.6 per cent showed malignant changes, again contrary to my observations. He considers x-ray even of less use than radium. In our experience sarcomata have been extremely radiosensitive.

The classification of ovarian tumors is based on 327 cases, including 100 simple cysts. It appears that there is much reduplication in the classification adopted by Meigs, although it does not differ greatly from the accepted classifications.

The chapter on metastases is of exceptional value.

The gross illustrations of the book unfortunately have been reduced too greatly, thus obliterating to a large extent their excellence. The photomicrographs are good and valuable throughout.

Although considerable literature is mentioned at the end of the chapter, the bibliographies are not sufficiently complete to permit of using the volume as a book of reference. The text is simple, clear, and easily read.

—R. T. Frank

This compact enumeration and description of all the actual and possible *Effects of an Accident on the Female Genitalia*,<sup>24</sup> as recorded in literature, evidently has been prepared for the benefit of gyneecologists, appearing as medical experts in German courts. They must possess and prove thorough familiarity with this complex problem. The small monograph deals in great detail with actual injuries and with possible relations of trauma to alterations in position and function of the nonpregnant uterus, and with its effects on an existing gyneecologic disease or pregnancy. In

<sup>23</sup>*Tumors of the Female Pelvic Organs*. By Joe Vincent Meigs, Instructor in Surgery, Harvard Medical School, etc. With 261 illustrations. The Macmillan Company, New York, 1934.

<sup>24</sup>*Weibliche Geschlechtsorgane und Unfall*. Von Professor Dr. August Mayer, Direktor der Univ. Frauenklinik in Tuebingen. 82 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

this latter respect even the influence of an accident on labor through resulting inertia or sear constrictions is considered. The monograph closes with a carefully prepared and classified list of bibliographic references.

—Hugo Ehrenfest

### Miscellaneous

This volume,<sup>25</sup> entirely free of any chauvinistic motive, attempts simply to show in how far medical men of the Jewish race have helped to bring American medicine to its present high rank. Chapter I briefly surveys earlier history and starts with the interesting statement that Columbus had with him five Jews, two of them being ship's physician and ship's surgeon respectively. There follows the listing of physicians, prominent in the author's judgment, each chapter devoted to a special field of medicine, closing with Chapter XV, in which are given the men who have written on the History of Medicine. One of the several appendices brings the description of all existing Jewish Medical Institutions.

The author prepared this comprehensive work by a personal study of all available medical literature and this fact probably accounts for two minor shortcomings: Some men, well known locally and nationally as outstanding clinicians and skilled operators but not given to writing, have been overlooked, while, on the other hand, the importance of others has become exaggerated through the number of their, often not very important, publications. However, there can be no doubt that this volume represents a very valuable contribution to the history of medicine in this country.

—Hugo Ehrenfest

The second edition of the *Standard Classified Nomenclature of Disease*,<sup>26</sup> compiled by the National Conference on Nomenclature of Disease, appears three years after the first. It has been accepted for use in the record rooms by 120 of the large hospitals in the United States and Canada and, as I can say from personal experience, appears in a large measure to solve the problem of classification. Some 2,000 additional items have been added so that at present it covers approximately 15,000.

Although at first sight confusing, the classification in practice works out well. Many omissions have been corrected and debatable points clarified.

It would be advisable for those hospitals which have not accepted the classification, to install it in their record rooms in order that the statistics of the entire profession in the United States be recorded according to the same formula and thus be more readily comparable.

—R. T. Frank

The main object of this book is to outline *Nursing Technique*<sup>27</sup> as taught in the Associated Hospitals of the University of Minnesota. The material, as in the previous edition, is arranged in lessons. It should prove of real value to teachers in training schools as well as to nurses preparing for examinations.

—R. T. Frank

<sup>25</sup>*Jewish Contributions to Medicine in America (1656 to 1934)*. By Solomon R. Kagan, M.D. With medical chronology, bibliography and 60 illustrations. 519 pages. Published by Boston Medical Publishing Co., Boston, 1934.

<sup>26</sup>*Standard Classified Nomenclature of Disease*. Compiled by the National Conference on Nomenclature of Disease. Edited by H. B. Logle, Executive Secretary. 870 pages. Commonwealth Fund, New York, 1935.

<sup>27</sup>*Textbook of Nursing Technique*. By Marlon L. Vannier, R.N., and Barbara A. Thompson, R.N., Director of the Wisconsin Bureau of Nursing Education, etc. Second edition, revised, 265 pages. University of Minnesota Press, Minneapolis, 1935.

## Correspondence

---

*To the Editor:\**

In the *American Journal of Obstetrics and Gynecology* of July, 1934, Dr. Ralph E. Campbell published an article, "The Effects of Chloral Hydrate on the Maternal and Fetal Organism from the Standpoint of Experimental Study." Dr. Campbell introduced into the stomachs of dogs, by means of a tube, 0.4 gm. of chloral hydrate per kilogram of body weight, and then, by very greatly increasing these quantities per kilogram, produced markedly detrimental changes in the liver, kidneys, and heart of these animals. Such results are quite comprehensible. It is acknowledged that chloral hydrate, as well as other powerful drugs, when taken in large doses, is poison to the organism. That is why pharmacologists classify doses as "medical" and "toxic."

Based on his observations on the toxic doses, the author concludes that chloral hydrate should not be used in cases of eclampsia. But this can hardly be regarded as correct. In the first place it is unreasonable to assume that the effect on healthy animals is the same as that on sick ones without definite clinical proof. In the second place, one cannot from the effect of toxic doses predict accurately the effect of medical doses, especially in eclampsia, when ordinarily we employ doses in strength one-tenth or even one-twenty-fifth of those used by Dr. Campbell. It might be more helpful if the author would investigate the influence on dogs of the dosage applied to women with eclampsia. But even then the conclusions could not directly be transferred to the dosage of sick people; healthy animals and sick animals react differently to medical treatment. How much more differently a sick man and a well man.

The experiments in the laboratory of Bezredko in Paris, on animals suffering from anaphylaxis, which has a distinct analogy with eclampsia, have shown that narcotics produced a marked improvement in the state of the experimental animals. The experiments of Anselmino and Hoffman, Küstner and Fauvet with animals injected with hormones from the posterior lobe of the hypophysis have also shown that narcotics have relieved the condition. It is known that these authors suppose eclampsia to be the result of the increased activity of the hypophysis. These authors acknowledged on the grounds of their investigations the prophylactic method to be the rational one. It can easily be explained theoretically. Eclampsia is a toxemia with convulsive attacks. These attacks have a very destructive effect on the organism. The toxemia itself can be fatal to a woman within a couple of months; the convulsive attacks can kill her in a day, sometimes in a few hours. Very strenuous methods are required to stop these attacks, and these measures have been, up to the present, the use of chloroform and chloral hydrate.

I do not wish to imply that it is unnecessary to look for other more effective and safer means to combat eclampsia; many such means have been proposed, including magnesium sulphate, luminal, pernocton, somnifen, avertin, and others. I know, however, that these narcotics in large doses poison the organism, and that with magnesium sulphate some fatalities have occurred. As for chloral hydrate, I do not know of any fatality following upon its use among 2,000 eclamptic patients in

---

\*The publication of Professor Stroganoff's letter was delayed to afford Dr. Campbell an opportunity to make a suitable reply. In view of the association of the former with the well-known conservative method of treating eclampsia, the publication of the original communication and Dr. Campbell's comments should prove of interest to the readers of the JOURNAL.

The Editors.

Leningrad. In short, my principal objection to Dr. Campbell's view is that clinical results must be given first place, and until the superiority of a drug is established clinically, it cannot be recommended for general use, but merely employed for experimental purposes.

Moreover, we cannot renounce the utility of the medicine which has given the best result in fighting a certain illness simply on the basis of experiments upon healthy animals. The best results in the treatment of eclampsia during the last thirty-seven years have been achieved by the prophylactic method; this is acknowledged in the reviews of my published works. For instance, Plass shows that of 5,976 cases of eclampsia treated conservatively only 11.1 per cent were fatal. More than half of these cases were treated by the prophylactic method or its variations. The statistics given in my own work are as follows: of 7,344 cases of eclampsia, treated by the prophylactic method and its variations, 9.7 per cent proved fatal. Of these, 1,400 were treated, with my participation, by the *improved* prophylactic method, and only 6 per cent were fatal. As to the 1,432 children in these cases, 79.7 per cent of them left the hospital alive.

These definite and proved statistics refute entirely the statement of Dr. Campbell about the harmful effects of chloral hydrate in the treatment of eclampsia. As for the measures he recommends, it is my opinion that investigations into the effects of  $MgSO_4$ , luminal, pernoeton, etc., would be valuable, but only if used in conjunction with the prophylactic method which is proved to be sound. Even so, it would be safe to recommend those measures *for general use only on the basis of clinical experiments on two or three hundred cases at the least, and only on the strength of a lower mortality rate in these cases than that which I have quoted above*. I regret that Dr. Campbell gives no statistics about the number of women suffering from eclampsia to whom barbituric acid derivatives have been administered, nor about the results received. I regret also that he does not tell us whether the animals to which these drugs were administered had previously been inoculated with the hormones of the posterior pituitary.

In conclusion I would like to express my opinion that if 1.1, 0.6, or even 0.4 gm. of chloral hydrate per kilogram of weight were introduced into the stomach of any woman with eclampsia, she would die within twenty-four hours.

PROF. W. STROGANOFF.

Leningrad, November 6, 1934.

---

#### COMMENT ON THE FOREGOING COMMUNICATION

*To the Editor:*

Professor W. Stroganoff's criticism of my report on chloral hydrate demands careful consideration.

Litzenberg has pointed out that there are two diametrically opposed groups in the treatment of eclampsia: the radicals who insist on emptying the uterus after the first convulsion, and the conservatives who claim that operative methods are not only unnecessary but actually harmful. Professor Stroganoff belongs to the latter group and his works have been monumental and important in producing a conservative influence.

The criticism of drug dosage in animal experimentation with its application to therapeutics in the human needs no defense. Pharmacology would be at a loss without animal experimentation, as one of its means of investigation. Then, too, pharmacology and toxicology have no fence between them for measuring effects by giving the dose at varying levels. Professor Stroganoff suggests that the dosage

applied to women in eclampsia be tried experimentally in dogs to study the effects. He fails to realize that in animals, to produce a physiologic drug effect comparable to that in the human, entirely different dosages must be used; and sometimes the animal dosage is several times the human dosage. An illustration would be morphine in the dog with its dosage several times that of the human to produce comparable physiologic effects.

Stroganoff points out that experimental conclusions cannot be carried from healthy to sick animals, to say nothing of man. This statement is more academic and theoretic than real. Experimental pharmacology and toxicology would be a great loss to therapeutics if this statement were true.

He reports beneficial results with narcotics in anaphylaxis and makes an analogy in this condition to eclampsia. Several investigators, Johnstone, Murray, Zweifel, Whitridge Williams, and others, have shown negative results; the positive results were attributed to the introduction of the products of placental autolysis; unautolyzed placental tissue gave no reaction. Furthermore, the occurrence of eclampsia with hydatiform mole cannot be explained by the hypotheses which depend on interagglutination or of anaphylaxis.

Professor Stroganoff mentions the observations of Anselmino and Hoffman, Küstner, Fauvet, and others, who attribute eclampsia to the activity of the posterior lobe of the pituitary, and on the grounds of their investigations favor its prophylactic treatment. Harvey Cushing, a noted authority, points out the invasion of the posterior lobe by basophilic cells from the pars intermedia, and other hypertensive states. Byrom and Wilson in most careful and well-controlled experiments were unable to confirm the pressor and antidiuretic effects in several preeclamptic and eclamptic patients as found by Anselmino, Hoffman, and others. Cushing's observation is dependent upon more information concerning the normal limits of basophilic invasion before the evidence is conclusive. Smith and Kunkel are not impressed by the findings mentioned by Cushing; so that in the last analysis Stroganoff is basing his conclusions upon experimental evidence which needs confirmation. DeLee points out that in hundreds of toxemia cases in which posterior pituitary was given during labor that only one woman developed convulsions and that even in this case their causation was very questionable. Schwarz points out that in his large series infundin was given freely without any apparent damage; it would seem once again to indicate that the part the posterior pituitary plays in the etiology of the late toxemias and eclampsia needs definite confirmation. Certainly at the present time no rational conclusion can be drawn in the treatment of eclampsia with pituitary medication.

Stroganoff calls attention to the fact that theoretical deductions are easy in eclampsia—I would say, true enough in most diseases—and he defines eclampsia as a toxemia with convulsions, saying that the latter are injurious to the patient and must be stopped. He states dogmatically that the only means of controlling the eclamptic attack is "up to now" by using chloral hydrate and chloroform. A critical examination of the literature as to the treatment of the eclamptic convulsions shows such contradictory evidence that this statement cannot be accepted. Various agents have been successfully used in controlling the eclamptic convulsions. Mendenhall, Lewis, Bleckwenn, and several others have reported excellent results in the control of the convulsions of eclampsia by sodium amytal. Beck's results in controlling the eclamptic convulsions with huge doses of morphine are convincing. Bleckwenn has had a wide experience with sodium amytal, having given over 2,500 injections to some 200 patients, over a period of a year and a half. One patient alone received over 300 injections during the year; careful studies of elimination in this case failed to reveal any accumulative effect or toxicity. Bleckwenn reported several cases of eclampsia in which the convulsions were readily controlled.

Mendenhall reported in his cases prompt and complete control of the eclamptic convulsions. Lewis' series of cases shows once again that the convulsions can be controlled by sodium amytal. Emge and Hoffman, and Bourne, Bruger, and Dreyer have shown that sodium amytal is not injurious to the liver or kidneys. In these series it has been shown that where morphine and chloral hydrate had failed to control the convulsions, sodium amytal was effective. It is interesting to note that sodium amytal has been just as effective in the control of convulsions of cocaine and strychnine poisoning as in the convulsions of tetanus, meningitis, and rabies. Luminal has been successfully used in the control of the eclamptic seizures by Katsutya, of Japan, who showed a decrease in maternal mortality of 15 per cent by substituting its use for chloral hydrate. DeLee has substituted other drugs for chloral hydrate and chloroform in the treatment of eclampsia. J. W. Harris, of the University of Wisconsin, has removed chloroform and chloral hydrate from his eclampsia treatment and has substituted sodium amytal. Solomons, at the Dublin Rotunda Hospital, has a substitution therapy for chloroform and chloral hydrate, using morphine as a narcotic.

The treatment of eclampsia, a disease of unknown etiology and distinctly empirical as to treatment, must advance with the replacement of old ideas and dogmas, as science offers something better. This does not mean that we should be constantly casting aside methods of treatment one for another; but it does mean that the treatment of eclampsia is so empirical that well-founded and reasonably basic ideas should be considered and perhaps tried in the light of a better treatment, not a new one. Progress in any line of treatment always entails a degree of stability; self-satisfaction with one's method of treatment may be contrary to progress; and inactivity as to the development of newer and better ideas is not synonymous to progress in any line of treatment. Then, too, it is hazardous for one to resign himself to the conclusion that any treatment in medicine is the last word in perfection. It is commendable always to be on the outlook for a better substitution therapy in the furtherance of a cure. A routine treatment may surrender as if nothing requisite is wanting; such a resignation is dangerous and at times precludes advances in treatment; indeed, I am unwilling to admit that Professor Stroganoff has the best treatment for the eclamptic convulsion in the use of chloral hydrate, even though this drug has been used for years and in a great many cases. I am willing to use other drugs which do not have the disadvantages of chloral hydrates and in addition control the convulsions.

The obstetric profession in the United States and in foreign countries should perfect an organization to study comparative values of the different methods of treatment in eclampsia. Directors of large clinics should be willing to adhere to rigid lines of treatment for comparative purposes with other clinics both in this country and abroad; when these procedures are carried out, statistics will then show something of real value for comparison. There is a lack of common terminology; there exist numerous and diversified treatments, and, as Solomons points out, autopsies should be obtained in all deaths to eliminate such errors of diagnosis as brain tumor, cerebral hemorrhage, tuberculous meningitis, syphilis, and other conditions which, at present, are factors of error in statistical mortality rates. Some obstetricians have been unable to approach Stroganoff's results even though adhering rigidly to his treatment. I feel that there is a lack of a common denominator in the classification of cases, interpretations, and methods of treatment.

A common practice in this country is to collect statistics on several hundred cases of eclampsia from numerous clinics and to determine the mortality rate with all kinds of treatment and variations, with a veritable hodgepodge of facts.

I feel certain that, if one of our large obstetric societies would assume responsibility for the study of the eclampsia problem both in the United States and abroad, valuable and useful information would result; and mortality figures would be reasonably dependable. International organization and cooperation could work out as well in eclampsia as it has in cancer. It seems to me that mortality figures as reported by the large clinics in relation to eclampsia should be held with a considerable degree of scepticism and suspicion as to accuracy.

Professor Stroganoff has reported excellent results in the treatment of eclampsia by the prophylactic method and its variations. He appears to conclude from a study of his mortality rate that chloral hydrate cannot be a harmful factor in his treatment. His reasoning seems to be based on the assumption that the mortality rate is the harmful index of chloral hydrate; in other words, the death or survival of the patients. It does not seem to me that the condemnation of a drug is of necessity dependent upon the death of the patient. Obviously many other factors must be considered, as already pointed out in the case of chloral hydrate.

The use of chloral hydrate is dangerous in heart disease in which the heart has already been strained by eclamptic convulsions. Aufrecht has pointed out that the use of chloral hydrate and morphine is particularly dangerous, a combination universally used in the Stroganoff treatment of eclampsia.

Jung has pointed out that large doses of chloral hydrate as used in the Stroganoff treatment may kill the fetus. I have shown experimentally in pregnant dogs that chloral hydrate has produced a deleterious effect upon unborn puppies.

In conclusion, it seems to me that experimental and clinical evidence would strongly justify the exclusion of chloral hydrate in the treatment of eclampsia.

RALPH E. CAMPBELL, M.D.

4117 Mandan Crescent,  
Madison, Wisconsin.

---

## Item

### American Board of Obstetrics and Gynecology

The results of the 1935 examinations given applicants for certification by the American Board of Obstetrics and Gynecology are as follows:

A total of 112 candidates were examined. Of this number, 88 were approved for certification; 22 failed to obtain passing marks (6 of whom were failed and 16 conditioned); and 2 did not complete their examinations.

Below is a list of the candidates approved for certification. These names were announced at the dinner held at the Hotel Traymore, Atlantic City, New Jersey, on June 12, 1935, terminating the Board's two-day examination period.

#### ALABAMA

DOUGLAS, GILBERT F., Birmingham  
GARRISON, JOHN E., Birmingham

#### CALIFORNIA

KANNER, H. M., Sacramento

#### CONNECTICUT

PERRINS, HARLAN B., New Haven

#### DISTRICT OF COLUMBIA

CROWLEY, JEROME F., Washington  
DARNER, HENRY L., Washington  
NOTES, BERNARD, Washington  
ROSS, JULIAN WALDO, Washington

#### FLORIDA

STRUMPF, IRVING J., Jacksonville



## GEORGIA

COLVIN, EMMETT D., Atlanta

## ILLINOIS

COOLEY, WILLIAM, Peoria  
 DAILY, EDWIN F., Chicago  
 MALCOLM, WILLIAM A., Peoria  
 SCHMITZ, HERBERT E., Chicago  
 TUCKER, BEATRICE E., Chicago  
 WHITACRE, FRANK EDWARD, Chicago

## IOWA

CROWDER, ROY E., Sioux City  
 RANDALL, J. H., Iowa City

## KENTUCKY

BARRETT, A. B., Lexington

## MASSACHUSETTS

BERLIN, MAURICE G., Boston  
 FINKEL, HENRY S., Boston  
 GWYNN, SAMUEL C., Worcester

## MICHIGAN

HUBER, CARL P., Ann Arbor  
 KENNEDY, ROBERT B., Detroit  
 KRETZSCHMAR, NORMAN R., Ann Arbor  
 WHITE, MILO R., Detroit

## NEW JERSEY

BINGHAM, ARTHUR W., East Orange  
 D'ACIERNO, PELLEGRINO A., Union City  
 WATERS, EDWARD G., Jersey City

## NEW YORK

ALDRIDGE, ALBERT H., New York City  
 BULLARD, EDWARD A., New York City  
 CLARK, CHESTER E., Syracuse  
 DAICHMAN, ISIDORE, Brooklyn  
 DAVIN, EDWARD J., New York City  
 DUNCAN, CAMERON, Brooklyn  
 FEINER, DAVID, Brooklyn  
 FINLEY, JOHN R., New York City  
 FISCHER, HENRY S., Brooklyn  
 FRIEDMAN, SAMUEL LOUIS, Brooklyn  
 GOLDBLATT, MYRON E., New York City  
 GREENE, HARRY J., Brooklyn  
 HALPERIN, JACOB, Brooklyn  
 HAWTHORNE, JULIAN, Rye  
 HENNESSY, JAMES P., New York City  
 HIESCH, AARON, Brooklyn  
 HUGHES, E. C., Syracuse

HURD, RALPH A., New York City  
 JUDD, JOHN W., Ithaca  
 KALDOR, JOSEPH, Brooklyn  
 KAMINESTER, SANFORD, Brooklyn  
 KLEEGMAN, SOPHIA J., New York City  
 KLEIN, HYMAN, Brooklyn  
 KRAUSHAR, SAMUEL, Brooklyn  
 LOBSENZ, JACOB M., New York City  
 LORBER, HERMAN, New York City  
 McMANUS, JAMES P., Hollis, L. I.  
 MALLIA, WILLIAM M., Schenectady  
 MEAGHER, WILLIAM C., Brooklyn  
 MERRIAM, MAXWELL S., Brooklyn  
 MUELLER, CHARLES W., Brooklyn  
 O'CONNOR, FRANCIS E., Kingston  
 REID, GEORGIA, New York City  
 ROGERS, JOHN F., Poughkeepsie  
 ROSENBERG, MAXIMILIAN, Brooklyn  
 SACKETT, NELSON B., New York City  
 SALZBERG, ABRAHAM H., Brooklyn  
 SCADRON, SAMUEL J., New York City  
 SCHONECK, F. J., Syracuse  
 SHIELDS, FRANCES E., New York City  
 SHIR, MARTIN M., Brooklyn  
 WEINTRAUB, FREDERICK, Brooklyn  
 WILSON, ROBERT A., Brooklyn  
 WINPFHEIMER, SEYMOUR, New York City  
 WRANA, JOSEPH, Glendale, L. I.

## NORTH CAROLINA

BRADFORD, WILLIAMSON Z., Charlotte  
 HAMBLIN, E. C., Durham

## OHIO

ABRAMS, S. B., Cleveland  
 KENNEDY, EDWIN P., Cleveland  
 ROBISHAW, ARTHUR W., Cleveland

## PENNSYLVANIA

HEPP, JOSEPH A., Pittsburgh  
 LAWS, GEORGE M., Philadelphia  
 MILLER, FORD A., Philadelphia  
 WILLIAMS, EDWARD F., Altoona

## TENNESSEE

RUCH, WALTER ALLWEIN, Memphis

## VIRGINIA

WILLIAMS, T. J., University

## WISCONSIN

DARLING, FRANK E., JR., Milwaukee  
 HORWITZ, JACOB, Milwaukee

## ONTARIO

HARRIS, LOUIS J., Toronto

For application forms and any information regarding coming examinations for certification, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pa.

---

### **American Board of Obstetrics and Gynecology Examination**

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, December 7, 1935.

Application blanks and booklet of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for this examination must be filed in this office not later than November 1, 1935.

---

On going to press we are informed of the death of Dr. Barton C. Hirst of Philadelphia. An extended obituary will appear in the October issue of the JOURNAL.

---

## Books Received

---

BIRTH CONTROL. ITS USE AND MISUSE. By Dorothy Dunbar Bromley, with an introduction by Dr. Robert Latou Dickinson. 304 pages. Harper & Brothers, New York, 1934.

PARENTHOOD, DESIGN OR ACCIDENT? A Manual of Birth-Control. By Michael Fielding, M.D. With 8 illustrations, 239 pages. The Vanguard Press, New York, 1935.

LA ROENTGENTHERAPIE DES FIBROMYOMES DE L'UTERUS, ET DE METROPATHIES HEMORRAGIQUES. Par Paul Gibert. Avec 10 figures dans le texte. 110 pages. Masson et Cie, Editeurs, Paris, 1935.

ECONOMIC PROBLEMS OF MEDICINE. By A. C. Christie, M.S., M.D., Professor of Clinical Radiology, Georgetown University, Medical School, etc. 242 pages. The Macmillan Company, New York, 1935.

FACIES DOLOROSA. Das Schmerzliche Antlitz. Von Dr. H. Killian. Mit 64 Abbildungen, 88 pages. Verlag von Georg Thieme, Leipzig, 1934.

DER UNVERMUTET SCHNELLE TOD IN SCHWANGERSCHAFT, GEBURT UND WOCHENBETT. Von Geh. Med. Rat Professor Dr. Erwin Kehrler, Direktor der Univ. Frauenklinik in Marburg. 52 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

LUNGENTUBERKULOSE UND SCHWANGERSCHAFT. Von H. Braeuning, Chefarzt der Fuersorgenstelle fuer Lungenkranke in Stettin, etc. 275 pages. Mit 391 Kurven und Abbildungen. Verlag von Georg Thieme, Leipzig, 1935.

JEWISH CONTRIBUTIONS TO MEDICINE IN AMERICA (1656 to 1934). With medical chronology, bibliography and 69 illustrations. By Solomon R. Kagan, M.D. 549 pages. Published by Boston Medical Publishing Co., Boston, 1934.

CLINICAL MANAGEMENT OF SYPHILIS. By Alvin Russell Harnes, M.D., Chief of Congenital Luetic Clinic, New York Hospital. The Macmillan Company, New York, 1935.

AIDS TO SURGERY. By Cecil A. Joll, Senior Surgeon to the Royal Free Hospital, etc., and Reginald C. B. Ledlie, Surgeon to Miller General Hospital. Illustrated by H. H. Greenwood, Consulting Surgeon, G. W. R. Hospital, Swindon. Sixth edition, William Wood & Company, Baltimore, 1935.

PHYSIOLOGIE UND PATHOLOGIE DER WEHEN. Von Dr. Tassilo Antoine, Assistent der Univ. Frauenklinik, Professor Weibel, Wien. Mit 43 Kurven. Verlag von Wilhelm Maudrich, Wien, 1935.

DISEASES OF CHILDREN. Third edition with contributions by 36 authors; edited by Hugh Thursfield, physician, Hospital for Sick Children, etc., and Donald Paterson, physician to out-patients, Hospital for Sick Children, etc. William Wood & Company, Baltimore, 1934.

THE WOMAN ASKS THE DOCTOR. By Emil Novak, M.D., Associate in Gynecology, Johns Hopkins Medical School. Illustrated by Carl Clarke. Williams & Wilkins Company, Baltimore, 1935.

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.

# American Journal of Obstetrics and Gynecology

---

VOL. 30

ST. LOUIS, OCTOBER, 1935

No. 4

---

## American Gynecological Society *Sixtieth Annual Meeting*

---

### THE CONTRIBUTIONS OF GREAT BRITAIN TO GYNECOLOGY AND OBSTETRICS

BROOKE M. ANSPACH, M.D., PHILADELPHIA, PA.

THE history of medicine is fascinating. In 1921, Walter Chipman, our president, eloquently portrayed the progress of gynecology in this country. He referred to the influence of Great Britain and traced the establishment of our oldest medical schools and hospitals to some of those Americans who finished their education in the universities of Scotland or England.

Great Britain figured largely also in the development of gynecology and obstetrics. Her contributions were of the greatest value and these, in compliment to our distinguished guest, I have chosen as the subject of my address.

To begin with, we may regard gynecology with obstetrics as a most important specialty. Fairbairn in a delightful preface to his textbook says, "Although to the life and the health of the individual the reproduction function is not essential, it is the very source of the life of the nation: hence the communal and sociologic aspect is relatively much more prominent in these subjects than in the other branches of medical science."

William Harvey was the first English writer upon obstetrics, and William Giffard was the first to publish substantial contributions.

The invention of the forceps by the Chamberlens had much to do with the rise of the accoucheur. Obstetrics as pointed out by Fairbairn

---

The articles contained in this issue are papers read at the Sixtieth Annual Meeting of the American Gynecological Society held at Hot Springs, Va., May 27 to 29, 1935.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

grew up somewhat outside the field of medicine and surgery. When manuscripts upon obstetrics first appeared in English, they were considered objectionable reading for anyone but midwives. There was also great prejudice against male help in labor, and this arose from the fact that since men were summoned only in emergencies, the child or even the mother usually perished.

In 1760, Elizabeth Nihell, the great champion of the midwives in England, published *A Treatise on the Art of Midwifery*, setting forth the objections to male help in labor. She directed her denunciation largely against William Smellie who is credited with being the founder of modern obstetrics in England.

Smellie (1697-1763) in his epoch-making work cleared up many misconceptions and superstitions which still enshrouded the whole theory of the practice of midwifery.

William Hunter (1718-1783), another famous Scot, was a contemporary of Smellie's and the brother of John Hunter. His book, *The Anatomy of the Gravid Uterus* (1774), is declared by Cutler to be "one of the most remarkable productions of the eighteenth century."

Special mention must be made of Charles White of Manchester, who, in 1773, observed the incidence of puerperal sepsis in private practice and noticed its contagiousness. He advocated certain principles, among them being cleanliness, ventilation, and chloride of lime disinfection. His pupils, Kirkland (1776) and Gordon (1775), corroborated his views and equaled his results.

"The English obstetricians," said Adami, "first found control over puerperal fever; they held to the contagious theory of the origin of the disease, said the condition was preventable and so must be prevented." Later these principles were lost sight of by the English school and their subsequent revival resulted from the work of Holmes and Semmelweis.

As we approach the year 1876 when this Society was founded, we enter the period of the greatest interest in the development of pelvic surgery. Here we encounter the men of Great Britain who left their indelible impress upon it, and especially Simpson, Wells, Lister, and Tait. Three of them were alive at that time. Simpson had died six years earlier, Wells had reached the age of fifty-eight, Lister was forty-nine, and Lawson Tait was thirty-one years old.

In estimating the influence of these men upon the development of gynecology, we must dwell for a moment on some of their contemporaries and take into account the state of medical science in that day. A retrospective glance carries us back to the art of surgery before the discovery of anesthesia, when the time consumed by an operation was of the utmost importance and the outstanding surgeon was the man who possessed the greatest amount of manual dexterity. Such a surgeon short-

ened the painful ordeal, and was in much demand whereas the man who "niggled" over an operation was avoided by the physician and the patient alike.

Possibly the most skillful surgeon of his time in England was Robert Liston, the friend and preceptor of Syme. An amputation of the thigh performed by this man, including the making of the flaps, the sawing of the bone, and the detachment of the limb, is recorded as having been accomplished in twenty-five seconds.

James Syme (1800-1870) was one of those who benefited by the discovery of anesthesia. So far as manual dexterity goes it was reported that he could not compare with his contemporaries, Liston and Ferguson, and that he left London and returned to Edinburgh where his deficiency would be less noticed. With the advent of anesthesia, Syme became an outstanding figure. Surgery no longer reached its height in mere rapidity of action; there was time for perfection in technique; new fields were opened for treatment, surgical pathology at last could be studied adequately, and the patient could be relieved of the horror of an operation.

Syme was appointed to the Chair of Clinical Surgery at Edinburgh in 1833. After visiting him in 1862, Marion Sims declared: "I have seen great surgeons operate all over the world, but I have never seen such an operator as Dr. Syme." Personally Syme was the embodiment of the old-fashioned gentleman. He dressed immaculately, and there never was any appearance of hurry in his manner.

In 1839, much against Syme's will, there was elected to the Chair of Obstetrics at Edinburgh by a majority of one vote a young man of humble origin, who was destined to figure prominently, James Y. Simpson (1811-1870).

Even as an undergraduate his brilliant mind and unusual energy had greatly impressed his teachers. His inaugural address delivered at the time when he received the doctors degree at the age of twenty-one attracted the attention of John Thomason, Professor of Pathology, who appointed Simpson as his assistant. Thomason later advised Simpson to specialize in obstetrics which was then looked upon with more or less disdain, believing that his kindly manner would fit him for the care of women in childbirth.

His attractive personality and ability as a teacher made the class in obstetrics the largest at Edinburgh for the first time in its history.

Simpson is credited with making the earliest systematic study of the diseases of women. The addition of chloroform to anesthesia (1847), the invention of the obstetric forceps that bears his name, and the discovery of acupressure as a means of controlling hemorrhage (1859) are among his achievements.

As early as 1848 he saw the frightful results of overcrowding and uncleanness among surgical patients in large hospitals and proposed

isolated smaller buildings that might be destroyed when they became a source of danger. His famous work on *Hospitalism* first appeared in 1867.

Simpson was a man of unusual appearance. Long tangled hair covered a head much above the average in size. His eyes, "sometimes piercing, sometimes almost feminine in tenderness," shone from under massive brows. His nose was coarse and had dilated nostrils. He had a strong jaw and a mouth "which seemed capable of being made at will the exponent of every passion and emotion." With his medium height, broad shoulders, short thick neck, and peculiarly rounded body and limbs, he was altogether a striking figure, and in any company commanding and impressive.

From the very beginning of his career he was the recipient of the highest honors; learned societies of every land paid tribute to his greatness.

He had much personal charm and there was no one in Great Britain who was more widely sought. "At his house," said Gross, "there was a constant round of hospitality." Interesting guests frequented his table and distinguished visitors came from a great distance. He was a ready and attractive conversationalist "brimful of accounts of great personages, ghosts, murders, and church affairs."

Up to this time ovariectomy in Great Britain as in other countries had made slow progress. Lizars in Edinburgh had performed the operation in 1825, and Clay of Manchester undertook it in 1842. The frightful mortality that followed its use aroused great opposition. Syme exerted his influence against it, and Simpson was unwilling to expose a patient to such a danger.

One of the most successful ovariectomists of his time was Isaac Baker Brown (1812-1873). He adopted methods which it is said "lowered the mortality to one-half." He dropped the pedicle, securing hemostasis by division with the cautery and ligatures cut short. Keith who succeeded Brown depended almost entirely on cauterization, performed slowly and with complete charring at the line of division.

Spencer Wells (1818-1897) an ovariectomist who acquired world-wide renown was seven years younger than Simpson and only twenty-eight when the discovery of anesthesia gave new impetus to surgical work. Although in 1854 he assisted Baker Brown with an ovariectomy he did not at that time approve of the operation believing that the risk of invading the peritoneal cavity was insuperable. During his experience in the Crimean War, he discovered the ability of the peritoneum to take care of itself. Two years after his return to England in 1856 he performed his first ovariectomy which proved a complete failure, but by 1880 he had done the operation one thousand times. His experience with this surgical procedure exceeded that of any of his competitors. In his

Bradshaw lecture in 1890 he reported 1,378 operations. Wells' ovariectomy clamp was finally discarded, and he contributed nothing to ovariectomy beyond such observations as accrued from the large number of operations he performed. Nevertheless he was its chief advocate and all the changes, the ebb and the flow of the development of the procedure centered about him.

The work of Brown, Keith and Wells must have influenced both Syme and Simpson in their views, for Syme in 1865 spoke of Wells' work and its promise for the future, and Simpson in one of his last lectures said that ovariectomy was a "fairly legitimate surgical operation."

There is little doubt but that the discovery of anesthesia hastened the development of pelvic surgery just as it enlarged the field in general. However, the prevalence of postoperative sepsis was frightful and interfered with a wide adoption of the operation as an established method of treatment. "Unhappily," says Allbutt, "this new enfranchisement of anesthesia seemed an ironical liberty of nature," who with the one hand gave and with the other took away what she had given.

The concept of the transmission of diseases was not new; it existed even from the remotest times as is shown in the writings of the ancients. But whatever had been said of the value of segregation and chlorinization was more or less disregarded by surgeons whose theories regarding wound infections remained extremely vague.

The surgical habits of the day provided the most excellent grounds for the propagation and transplantation of hospital diseases and "no shame was felt for the good old surgical stink that at all times pervaded hospital wards" (Godlee).

The prevailing state of mind relative to surgical cleanliness is shown by the following circumstance: When Isaac Baker Brown lost a patient in 1854, he said to Wells who had assisted him in the operation, "it's the peritonitis that beats us." Although he recognized the evil he could scarcely have grasped its significance for a year (1869) after his book on ovariectomy appeared, he brought out one on "Scarlatina" in which he carefully described his plan of making applications to the throat.

It is a remarkable fact that Brown lost 26 of his first 50 patients and only 4 of his last 50; this great improvement he attributed to the method of treating the pedicle. One cannot help but wonder whether without realizing its importance, he had adopted some other measure also that prevented the transmission of infection from his scarlet fever to his surgical patients. Whatever the true explanation may be, his success began in 1865, the year in which Lister inaugurated his principles of antisepsis, an innovation that changed the whole complexion of surgery.

The epoch-making work of Joseph Lister (1827-1912) must not be regarded as merely the practical application of the discoveries of an-



other; it was rather the culmination of many years of study and inquiry, as to the origin and the morphology of inflammation. He had long sought for an explanation of postoperative morbidity and mortality in the hope that in some way they might be lessened or prevented. With his thorough understanding of the most pressing question that had to do with surgery "he was watching from the heights" as Allbutt has expressed it and immediately saw in Pasteur's discoveries the answer to his problem.

The photographs of Joseph Lister show a broad high forehead, a finely chiseled nose of good proportions, a well-formed chin and a wide expressive mouth. His manner was dignified and this aroused in younger men and women who did not know him a certain amount of awe. To them he might appear solemn and devoid of a sense of humor; but his intimates knew that he appreciated wit as well as any one, although he was intolerant of irreverence or vulgarity.

His students, house surgeons, and assistants idolized him: there sprang up quickly an affectionate regard for the "chief" which they felt was returned.

To his patients he was interested and sympathetic in his attention: his gracious manners and his thoughtful mien gave one an impression of power and resource, a mastery of the situation and a preparedness for "those possible emergencies that haunt the minds of nervous patients."

About the time that Lister began the use of carbolic acid, another figure appeared that was destined to loom large on the surgical horizon. It was that of Lawson Tait (1845-1899) whom William Mayo styles "the father of abdominal surgery." Tait had been an assistant and close associate of Simpson's as early as 1862 and had served also with Syme. He was only twenty-three years old when he boldly essayed the then highly dangerous operation of ovariectomy.

Tait was reluctant to accept the principles advocated by Lister, and abandoned them after a brief half-hearted trial. He greatly admired Syme, the father-in-law of Lister, and from the very first adopted some of the habits of Syme in his surgical work, namely, those of neatness and cleanliness, not only in his person, but also in the conduct of his surgical wards.

Tait soon passed beyond the limitation of ovariectomy to ovarian tumors and was the first to perform the operation for other reasons, removing in February, 1872 the slightly enlarged ovary of a woman who had suffered with pain.

It was not long after (August, 1872) that Robert Battey of Georgia removed both ovaries from a woman with an infantile uterus who had no menstrual flow but suffered with recurring and painful menses; Battey suggested the employment of his operation also for the purpose of

arresting menstrual hemorrhage in myoma uteri, and for the relief of certain nervous symptoms that defied all other methods of treatment.

Wisdom and moderation governed Battey's own use of what he termed "normal oophorectomy" as was evidenced at the International Gynecological Congress in London in August, 1881 when he stated that in his entire experience he had found only 16 cases in which he felt justified in performing this operation. In reviewing the discussion, the *Medical Times and Gazette* expressed surprise that Battey himself had had so small a number of cases, whereas Tait and Savage reported more than a hundred from Birmingham. The views of the debators were scarcely to be reconciled, but as was revealed later, Battey and Tait were discussing different procedures.

Tait was removing ovaries but what was more important, he was also removing diseased tubes. Up to this time inflammation outside the uterus was generally believed to have its seat in the cellular tissue, but Tait revealed the part it played in the pathology of the tubes, and performed salpingo-oophorectomy.

By 1888, Tait's views relative to the incidence and morbid anatomy of tubal disease as well as his aseptic surgery had received recognition on both sides of the Atlantic. Nevertheless there still existed some skepticism concerning the frequency of salpingitis, and some confusion between oophorectomy and salpingo-oophorectomy.

As indicating this state of affairs reference may be made to a letter of inquiry from J. Henry Carstens to the editor of the *American Journal of Obstetrics* in 1883 asking for information concerning the difference between Battey's operation and Tait's operation.

A noteworthy achievement and a milestone in the advance of gynecology was the immediate operation for ruptured tubal pregnancy, a procedure which Tait was the first to perform in 1883. A series of 35 cases with only two deaths speedily followed.

Physically, Tait was a short broad-chested and bulky man; like Simpson he had a large head and long hair, and between them there was great resemblance. His face was grave and plebeian. His hands were short and broad also like Simpson's, but whereas Simpson's fingers were said to taper, Tait's were quite the reverse. So far as appearances went it would have been difficult to imagine more unsuitable hands.

What he had to say he put in as few words as possible, and when he spoke his lips hardly moved. "He was a severe and formidable critic of loose thinkers and careless writers." He was opposed to the germ theory and to vivisection. His conclusions upon a subject were based upon his deductions made from a practical standpoint. He had no imagination, no scientific bent. Some men, said McKay, his biographer, have a love of truth so innate that in an argument the demonstration of the truth gives them greater satisfaction than the proof that their op-

ponents are wrong; but it was otherwise with Tait, for he gloried in the utter discomfiture of his opponents.

He was a bold and fearless surgeon but not rash. To his assistants he appeared equal to any occasion and created a feeling of confidence.

These men were giants sprung from British soil. We marvel at their industry and pay tribute to their achievements. As we reflect upon their lives so filled with moving events, we understand more clearly the difficulties they surmounted and the influence they exerted.

We need go no further. The successors of these men inspired by the examples set before them have carried on the torch of medical progress in Great Britain. They have contributed their full share to the warp and the woof of gynecology, woven by workmen from all quarters of the world. We know and gratefully acknowledge their accomplishments.

James Harvey Robinson in his book *The Ordeal of Civilization* says that in history the important point is a "realization of how things came about."

"This realization opens our eyes wider upon matters as they now stand and at the same time suggests more ingenious ways of forwarding their improvement."

---

## A STUDY OF A NEW AND POTENT ERGOT DERIVATIVE, ERGOTOCIN

FRED L. ADAIR, M.D., M. EDWARD DAVIS, M.D., M. S. KCHARASCH, PH.D.,  
AND ROMEO R. LEGAULT, PH.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, and the Department of  
Chemistry, the University of Chicago)

### INTRODUCTION

THE writers have reported already their adaptation of a method of study of uterine motility previously utilized by others, including Bourne and Burn, Moir and Rucker. This method was used in observations of the action of various drugs supposed to affect uterine contractility. The effect of some of these therapeutic agents was presented before the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons in September, 1933. Among these observations were some upon ergot. They were made mostly upon the uterus in the immediate postpartum period.

Our interest in this work was to evaluate the utility of ergot preparations and of the pure ergot alkaloid in obstetrics. It is well known that many of the ordinary fluid extracts prepared by many pharmacopoeial methods are unreliable in their effects. This has been a debatable issue for many years. It was assumed that ergot preparations contained some

principle which in time underwent deterioration. Innumerable attempts had been made to stabilize these preparations. All of the methods had as their objective the preparation of an extract uniform in effectiveness when assayed by either the pharmacopeial or the Broom-Clark methods. Some means of stabilization of ergot included the addition of reducing agents, the control of hydrogen ion concentration, exclusion of oxygen, etc. If one bears in mind what we know now of the active principle of ergot, namely ergotocin, it is obvious that the real difficulty was not always with the ergot preparations but with the various standard methods of testing ergot potency. In 1932, Moir suggested that the aqueous B.P. extract of ergot contained a substance which when given by mouth produced a prompt oxytocic action. He claimed that the activity of the aqueous B.P. extracts could not be due to the known alkaloids, for the concentration of these alkaloids in this preparation was too low. He further claimed that the aqueous B.P. extract was a reliable drug. In the light of our present study, this statement of Moir is not entirely correct, in that the potency of a preparation of ergot is dependent on the amount of ergotocin contained in the crude drug as well as upon the method of extraction.

Early in 1932, Prof. M. S. Kharasch and Dr. R. R. Legault undertook a study of the chemistry of ergot under a grant from the Research Corporation. It was natural that they should become interested in the principle responsible for the oxytocic activity of ergot and a cooperative study of the problem was undertaken by the two departments. The first step in our investigation was to separate the defatted ergot into two fractions, one containing the known alkaloids ergotamine, ergotoxine, sensibamine, ergoclavine, and most of the debris, the other fraction containing the unknown oxytocic substance or substances. This was evident from the fact that the first fraction showed little and variable activity; the second fraction which we designated as nonalkaloidal to distinguish it from the portion containing the known alkaloids included ingredients which gave uniformly typical ergot responses. Thus, early in our investigation it was evident that the typical oral oxytocic effect of ergot did not reside in the known alkaloids, a fact later corroborated by a study with the pure alkaloids. We have fractionated this "nonalkaloidal" fraction and tested the activity of the different materials. The potency of these fractions was always carefully checked by their administration to the puerperal woman. A careful kymographic record of its action was made in each case. Thus, chemical progress was always controlled by pharmacologic assay on the human subject. After many months we finally arrived at an ingenious technic for rapidly obtaining a new active principle in almost pure form, suitable for therapeutic administration from this crude nonalkaloidal fraction.

These studies of ergot and its various components were reported in November, 1934, at the meeting of the Central Association of Obstetricians and Gynecologists. We described the new active principle isolated from ergot and some of its chemical, pharmacologic, and clinical properties. It was found to be very active in doses of 1.2 to 3 mg. when administered orally. It was unlike the known alkaloids of ergot, chemically and pharmacologically. It was, undoubtedly, responsible for the major oxytocic activity exhibited by the drug.

Early in December of 1934 we finally isolated this new active principle in crystalline form. These crystals were found to be therapeutically active in doses of less than 0.1 mg. when given intravenously. We have agreed to call the new substance "ergotocin." Since that time we have continued our studies of this interesting new active principle and corroborated all the results previously reported. We have likewise

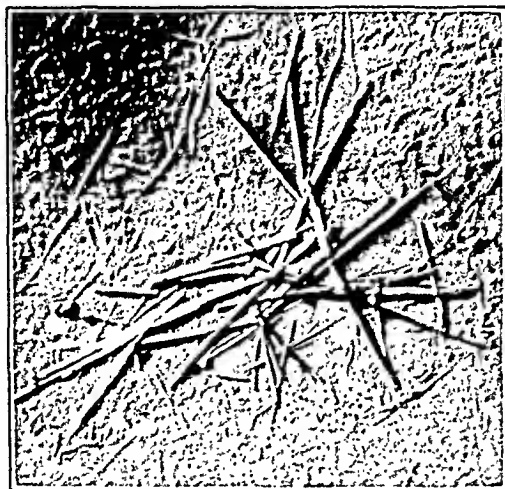


Fig. 1.—Photograph of crystals of ergotocin maleate.

progressed with a thorough chemical, pharmacologic and clinical study of ergotocin. Dudley and Moir, in March, 1935, reported the isolation of an active oxytocic principle from ergot.

#### CHEMISTRY

The empirical formula of ergotocin is  $C_{21}H_{27}N_2O_2$ . It is a colorless, crystalline material, appreciably soluble in water, imparting to the latter a weak alkaline reaction. It may be crystallized in long, fine needle-shaped forms from such solvents as chloroform, benzene, and trichloroethylene, but not from hydrophylic solvents such as alcohols or ketones (Fig. 1). When ergotocin is heated in a melting point tube, it begins to darken at  $155^{\circ}$  C. and melts sharply with decomposition at 159 to  $160^{\circ}$  C.

Ergotocin is very soluble in the lower membered aliphatic alcohols. It is only slightly soluble in nonpolar solvents, such as benzene, ethers, etc. It is very soluble in dilute aqueous solutions or organic or mineral acids. Solutions in dilute polybasic aliphatic organic acids are stable at ordinary temperatures and

may be sterilized at the boiling temperature of water without an appreciable loss of oxytocic activity and without imparting color to the solution.

In contrast to the behavior of the known ergot alkaloids, ergotocin in the form of the free base or as a salt is not precipitated from solution by the addition of Mayer's reagent in a dilution exceeding one part in six thousand whereas, under the same conditions, the ordinary ergot alkaloids are precipitated in a dilution of one part in a million or more.

Ergotocin gives a blue color, in acid solution, with paradimethyl aminobenzaldehyde. It also gives a blue color with Folin-Denis' phenol reagent.

The ultraviolet absorption spectrum of ergotocin is very similar to that of the known ergot alkaloids. The difference is one of degree rather than of kind. There is a minimum at 2700  $\text{\AA}$  and a maximum at 3100  $\text{\AA}$ . It is interesting to note that it has a very high coefficient of absorption of light in the region of the ultraviolet. However, in the region bordering the visible, practically no light is absorbed.

In contrast to the known ergot alkaloids, ergotocin does not give off a molecule of ammonia when treated with alkali. However, under alkaline hydrolysis a product is liberated which appears from all properties so far examined to be identical with lysergic acid.

Ergotocin forms well-defined crystalline salts with certain polybasic acids. These acids include the aliphatic polybasic acids and phosphoric acids. The monobasic and other mineral acids do not form crystalline salts with ergotocin. The salts of the polybasic acids have no characteristic melting points; they decompose within a short temperature range.

As would be expected, ergotocin is optically active. It is levorotatory and its salts are dextrorotatory. The specific rotation of the maleate in water is approximately  $+77^\circ$ .

The question whether ergotocin is an alkaloid or a nonalkaloid is a trifling one. In our previous contribution we stated clearly the criterion we used for describing what we termed the nonalkaloidal portion of ergot, from which ergotocin was finally obtained, and also what we termed the alkaloidal fraction which contained the so-called "known ergot alkaloids."

We wish to clarify our position and statements and are incorporating a short analysis of the status of the chemical opinions regarding alkaloids.

The term "alkaloid" was recommended at a time when very little of the chemistry of naturally occurring substances was known, and it was based mostly on a limited knowledge of the field and a limited vision on the part of the originator of the word. A quotation from Henry's book, *The Plant Alkaloids*, is most pertinent. It indicates how loosely the term could be used and how difficult and unreliable, and therefore uncertain in its meaning, it is to term naturally occurring nitrogenous substances alkaloids, or nonalkaloids.

The word alkaloid was at first used to describe all organic bases, including the natural alkali-like substances which occur in plants. At the time this name was introduced comparatively few of these latter substances were known, and these were all alike in possessing basic properties and in exhibiting physiologic activity. These two characteristics, in conjunction with their complex structure, have made it possible until recently to regard the natural alkaloids as forming a well-differentiated group of chemical compounds, but recent work has tended to render indistinct the border lines between this and other groups. On the one

hand, such simple basic substances as ammonia and methylamine, and on the other, substances that contain nitrogen and are yet acidic rather than basic have been found in plants. And, again, complex substances closely related to typical alkaloids and which must be regarded as belonging to the class of alkaloids, though they have no marked physiologic action, are known. König proposed to avoid this difficulty by confining the name alkaloid to naturally occurring pyridine derivatives, but this rules out such important substances as the purine and glyoxaline derivatives, and for that reason can hardly be accepted as a satisfactory use of the name.

One must bear in mind that since this work of Henry has appeared, a number of simple nitrogenous substances, such as amino acids, have been isolated from plants, for instance, asparagine, etc. Are these substances to be classed as alkaloids? Other authors define the term alkaloids as "basic substances occurring in plants which contain in their constitutions pyridine, quinoline, isoquinoline or pyrrol or pyrrolidine ring, or several rings." If this is used as a basis of classification, it is obviously impossible to state whether a substance is an alkaloid or not, until the complete chemistry of the substance is known. The present authors have always deplored the indefiniteness of the term alkaloid and prefer to speak of the chemical substances by their chemical characteristics rather than by their source or origin, or loose empirical classification. However, in our laboratory, and in some of the papers we have published, we have found it convenient to restrict the term "alkaloids of ergot" to substances which will give a precipitate with Mayer's reagent in a very high dilution, such as 1:200,000 or 1:1,000,000, and not necessarily to all nitrogenous substances that occur in ergot. For otherwise, on the basis of some definitions, we would have to apply the term alkaloid to the following nitrogenous substances which have been isolated from ergot: leucine, isoleucine, valine, tyrosine, histidine, trimethylamine, putrescine, cadaverine, isoamylamine, tyramine, histamine, agmatine, choline, acetylcholine, betaine, ergothioneine, uracil, guanosine, vernine, secale, amino-sulphonic acid. We believe that such a classification as we have adopted is perfectly valid in the restricted sense used by us. If the criterion we have outlined, namely, precipitation with Mayer's reagent, is used, then we have a perfect right to speak of alkaloidal and nonalkaloidal fractions in that sense, or certainly until the structure of the materials is definitely established.

With the isolation of the active component responsible for the oral effectiveness of ergot, and the establishment of its empirical formula,  $C_{21}H_{27}N_5O_3$ , the entire question whether the active principle is an alkaloid or nonalkaloid loses its argumentative appeal except for non-chemists. We have shown definitely that ergotocin is not precipitated by Mayer's reagent in a dilution higher than 1:6,000, while ergotoxine, ergotamine, and sensibamine are precipitated by that reagent in dilutions as high as 1:2,000,000. This is a unique characteristic which,

according to our definition and that used also by many other chemists, would differentiate alkaloidal from nonalkaloidal materials. We reiterate that the entire term alkaloid has outlived its usefulness and carried no meaning whatsoever, and it is high time that the term either be rigidly defined or be given up altogether.

In all of our future communications we shall dispense completely with that term and speak of ergotocin as a definite chemical compound rather than as an alkaloid or nonalkaloid. This decision is based upon our belief that the term alkaloid has lost completely its original meaning. It is loosely used and does not carry a definite concept, except as "a substance contains nitrogen," and the whole argument is much ado about nothing. We prefer not to use a word for the classification of chemical substances that cannot be rigidly and uniquely defined.

#### PHARMACOLOGY

*Experimental.*—The pharmacologic studies on animals have been carried out largely by Chen and Swanson. This has been published elsewhere. The general conclusions from work done in experimental pharmacology are: that this principle, ergotocin, has a powerful oxytocic action on both isolated and puerperal mammalian uteri; that the methods of the assay of ergot need revision. The U.S.P. cocksecomb method is not specific. Coeks developed gangrene of the comb when injected daily with 1 mg. of ergotocin. It is more potent gram for gram than ergotoxine. The reactions obtained in the cocksecomb by ergotocin, ergotoxine, and fluid extract of ergot, are indistinguishable. Unlike ergotamine or ergotoxine there is little inhibitory action on epinephrine by ergotocin, hence the Broom-Clark method is not applicable.

The isolated uterine response may be used as a method of assay inasmuch as the uteri both of virgin guinea pigs and of rabbits react to ergotocin. The former appears to be more sensitive but the latter seems to be more reliable. The postpartum uteri of dogs respond to tests made following the introduction of a hydrostatic bag.

Its toxic action is minimal. In the form of a maleate, ergotocin was found to have a minimal lethal dose of 250 mg. per kg. in mice and of 80 mg. in guinea pigs. When injected intravenously tetanic convulsions preceded death in these animals. No toxic symptoms were manifested in two dogs which were given 1 mg. per day for twenty days, though one had an evanescent albuminuria. The effect on involuntary muscles was shown by the production of mydriasis in a rabbit's eye, by constriction of a frog's limb vessels, and the relaxation of isolated rabbit's small intestines which latter effect can be abolished by the previous application of ergotamine. This behavior may indicate some stimulating action on the sympathetic endings. Ergotocin sometimes causes a pressor action



in pithed cats but produces a depressor action in anesthetized animals. Large doses suppress respiration. The metabolic rate is increased in white rats by intravenous injections of this agent.

*Human.*—Most of our studies are based upon observation of the sixth- to eighth-day postpartum uterus by the method previously described. We have used varying doses administered by each of the following methods: oral, sublingual, intramuscular and intravenous. The graphs illustrating the kymographic tracings of uterine contractility following the oral, sublingual, and intramuscular administration of ergotocin are similar and comparable. It is outstanding that the tracings derived from uterine contractions following its intravenous administration are markedly different, are typical and unlike any tracing we have obtained from any other oxytocic agent.

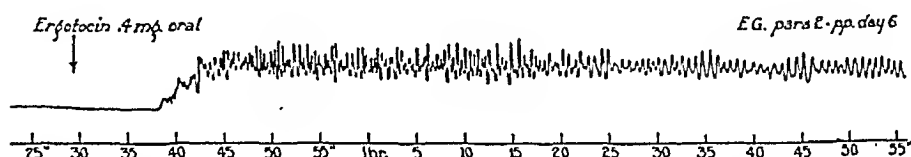


Fig. 2.—Graph obtained ten minutes after the oral administration of 0.4 mg. ergotocin. The stepladder-like rise of the curve shows the development of tetany. The contractions occurred every fifteen or twenty seconds, gradually becoming further apart at the end of the first hour. Uterine motility still persisted at the end of two hours.

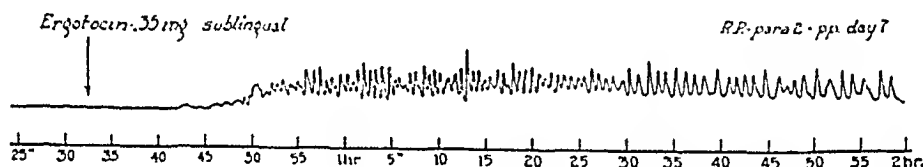


Fig. 3.—Graph obtained following the sublingual administration of 0.35 mg. of ergotocin.

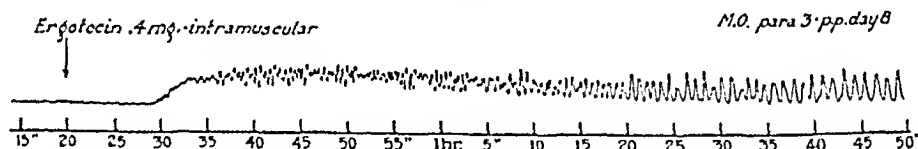


Fig. 4.—Graph obtained after the intramuscular administration of 0.4 mg. ergotocin. Note that the induction period is almost as long as by the oral route.

The tracings following the oral, sublingual and intramuscular administration of ergotocin are so similar that one description will suffice for all (Figs. 2, 3, and 4). The individual variations in these tracings may be accounted for by the variability in the reactions of the uterus of individual patients. The effect of the administration by these methods is not shown on the tracings for about eight to twelve minutes following its administration. The first noticeable effect is in the onset of slight contractions with a gradual increase of tonicity. This increased tone is clearly shown by the gradual ascent of the curve. The excursions of the needle show a gradual increase in the amplitude of the waves, indicating more marked uterine contractions. Not all of these contractions are of uniform strength, but they seem to run more or less rhythmically in groups of weaker and stronger contractions. At first the time interval between these contractions is longer, but this gradually becomes shorter. These frequent waves of contraction are maintained at a fairly constant tonicity level after the maximum tone is once attained. After a lapse of about forty minutes the contrac-

tions become less frequent, but the amplitude remains about the same with the corresponding tonic level. The tracing shows a diminution in both the amplitude of the contractions and the uterine tone after about an hour and a half, though there is evidence of continued uterine motility for three or more hours after the initial administration of ergotocin.

In striking contrast to the graphic tracings just described are those following the intravenous administration of ergotocin (Fig. 5, A, B, C). Here again there is slight variation in the tracings derived from individual patients, but in all of the tracings there are striking and typical characteristics. The relatively inactive uterus shows sudden activity almost instantaneously after the administration of intravenous ergotocin. This is demonstrated by the almost vertical

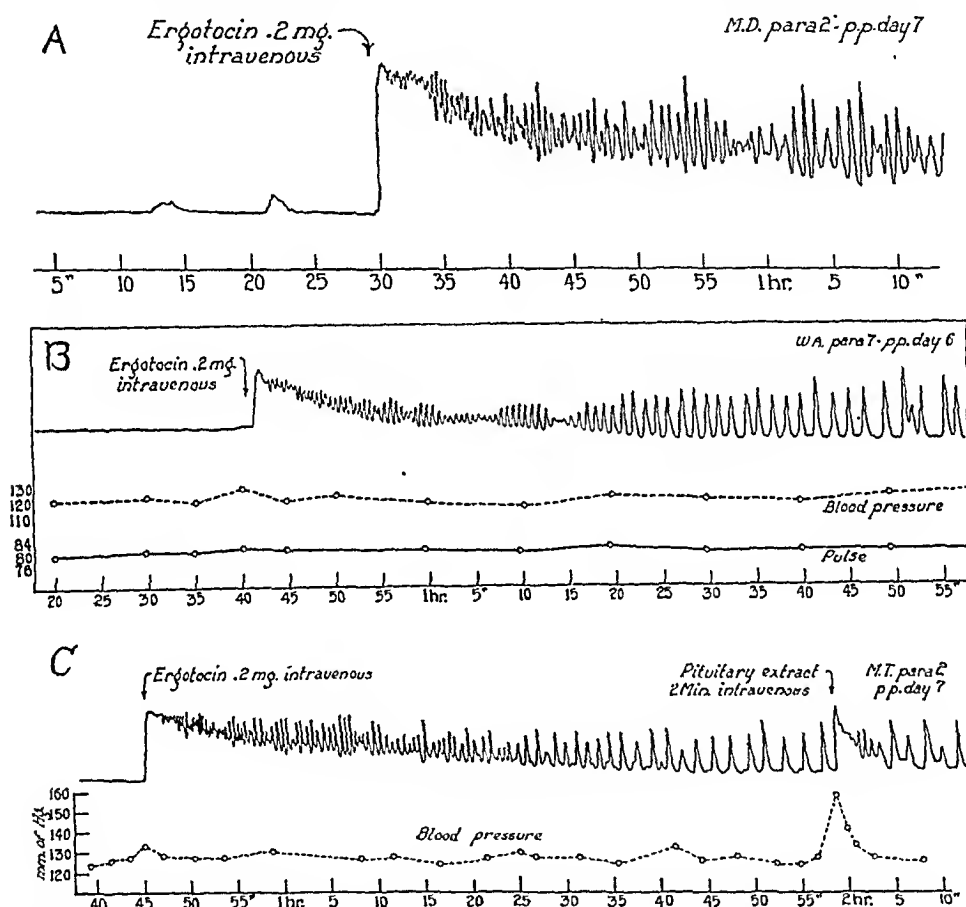


Fig. 5.—A, B, C, Graphs obtained following the intravenous administration of 0.2 mg. ergotocin. The almost instantaneous response of the drug is demonstrated by the abrupt rise of the curve fifteen or twenty seconds following the administration of the drug. Note the marked tetany which persisted for several minutes, after which tiny contractions began. These increased as the uterus gradually relaxed. Good tetany and motility were maintained for several hours.

ascent of the needle. This ascent occupies not more than fifteen seconds, at which time the tracing indicates that the uterus has reached its maximum tetany. Following this tetanic contraction the uterus begins to show slight intermittent contractions, the maximum point of which remains more or less at the maximum point of tonicity. The lower point of the contraction wave is below the level of the maximum tonicity but much above the level of the uterine tone prior to the administration of ergotocin. The tetany of the uterus gradually diminishes. The contractions imposed upon the tetanic state are at first of very low amplitude but gradually show more marked contractions and relaxations. The re-

maining portion of the tracings shows characteristics similar to those already described for the other methods of administration. The duration of the effect of this oxytocic agent continues for about the same length of time by all methods of administration.

We have previously called attention to some of the uterine reactions following the administration of large doses of ergotoxine ethane-sulphonate, ergotamine tartrate and sensibamine. We have given these drugs in doses of 3 mg. and more orally. The uterus remained relatively inert, following the administration of these alkaloids, for three-quarters of an hour and over (Figs. 6 and 7). In order to test the efficacy of ergotocin as compared with these agents in the same patients, we later administered ergotocin in approximately 0.4 mg. doses, both orally and sublingually, and have been able to secure the typical tracings previously described for this active principle. The administration of these alkaloids in large doses (2 or 3 mg.) by subcutaneous and intramuscular methods, while in some instances provoking uterine responses, did not excite uterine contractions to anything like the degree which was obtained by the use of ergotocin in much smaller doses. Furthermore, unpleasant reactions on the part of the patient, such as nausea, vomiting, and associated symptoms, occur from the former.

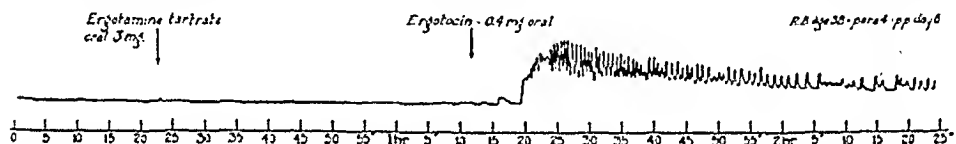


Fig. 6.—Ergotamine tartrate, 3 mg. orally, produced no contractions at the end of fifty minutes. About five minutes after the oral administration of 0.4 mg. of ergotocin a typical "ergotocin response" developed.

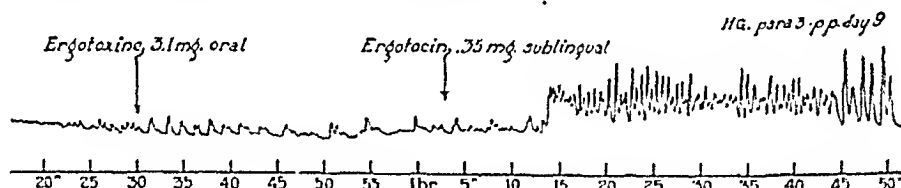


Fig. 7.—Ergotoxine, 3.1 mg. orally, produced no contractions at the end of one hour. About five minutes after the sublingual administration of 0.35 mg. of ergotocin a typical "ergotocin response" was obtained.

The difference in the uterine motility brought about by the administration of pituitary extract has been previously stressed. While the effect is perhaps equally prompt, the duration of increased uterine tone and contractility is very much shorter following the administration of pituitary extract than it is following the use of ergotocin.

The dosage of ergotocin is minimal. Effects are obtained by less than 0.05 mg., but the best response is obtained by the intravenous administration of approximately 0.2 mg. About twice this amount is used for other methods of administration. In a few cases slight nausea, with or without vomiting, is incurred, but such reaction is unusual. Much larger doses have been given without unpleasant manifestations. While the margin of safety is very wide, we feel that the minimum uniformly effective dose should be used.

#### THERAPEUTIC EFFECTS

Inasmuch as the unfavorable effects of the administration of some other oxytocics, such as pituitary extracts, upon blood pressure and urinary output are known, we have felt it necessary to observe some of

these reactions upon the patients who have received ergotocin. We have observed these results in a considerable number of cases, some of whom were apparently normal and others of whom presented definite evidence of disturbed vascular balance with marked hypertension. In a group

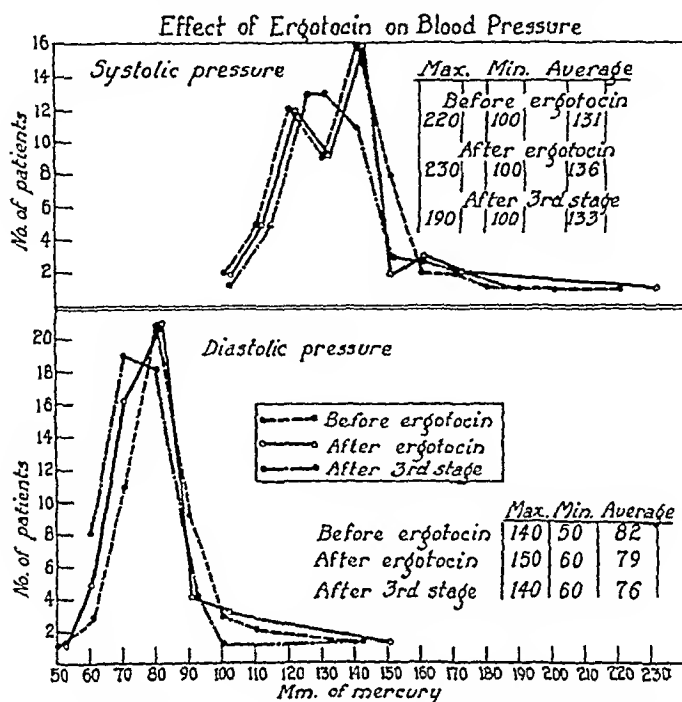


Fig. 8.—Graph showing the effect of ergotocin on the blood pressure.

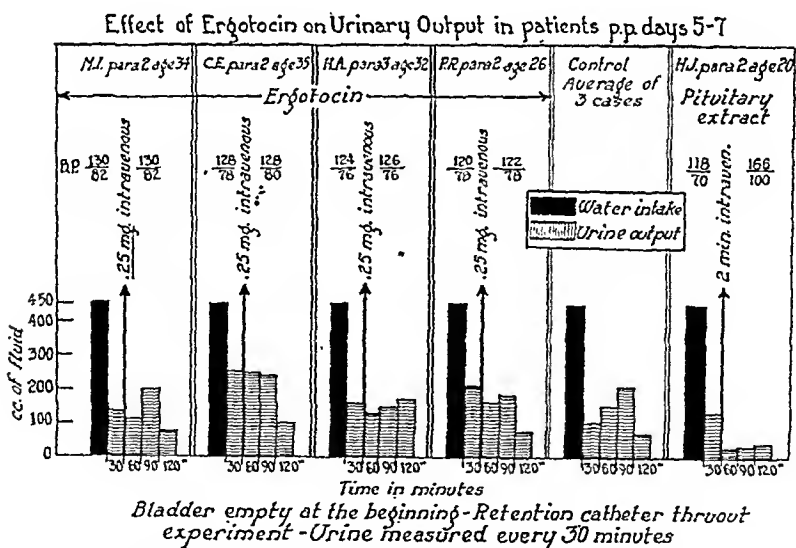


Fig. 9.—Graph showing the effect of ergotocin on the urinary output.

with no evidence of cardiovascular renal diseases, we found the average blood pressure before the administration of ergotocin was 129/80. The maximum blood pressure was 142/100 and the minimum was 100/50. The corresponding readings following the administration of ergotocin were 129/79 as an average, 148/100 for the maximum, and 100/56 for

the minimum. In the other group, with abnormal blood pressures, the average reading was 162/92, the maximum was 220/150, and the minimum was 144/70, before the administration of ergotocin. There was little change following the use of this drug as the average, maximum, and minimum are seen to be at approximately the same level (Fig. 8). We feel justified in concluding that both the patients with normal and those with abnormal blood pressure show little or no alteration as a result of the administration of ergotocin. This is a very important fact inasmuch as most oxytocics, notably pituitary extract, have a tendency to produce marked rise in blood pressure which action has inherent dangers, especially in patients with a disturbed vascular balance.

We also observed the effect of this drug on urinary output. Twelve cases were tested during the postpartum period. The bladder was emptied by means of a retention catheter. The patient was then given

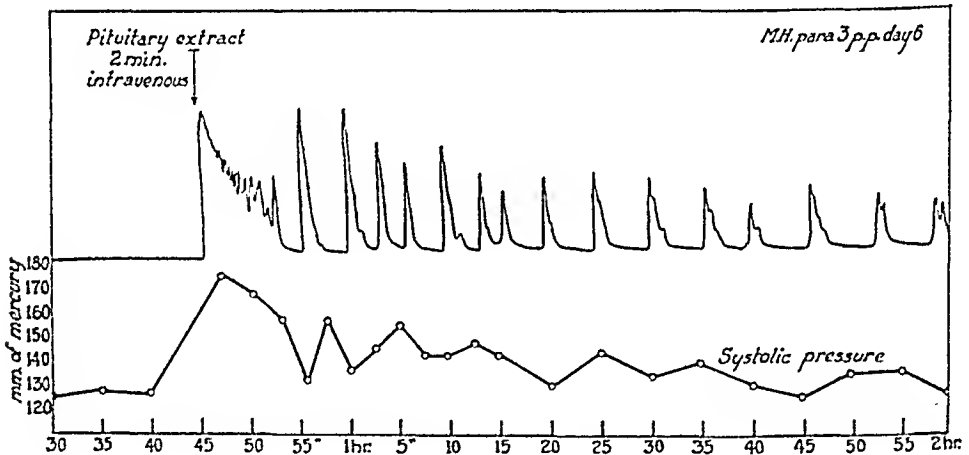


Fig. 10.

450 c.c. of water by mouth. The urinary output was measured thirty minutes later when 0.5 mg. of ergotocin were given intravenously, following which the blood pressure, pulse and pupillary reactions were observed. There were no alterations in blood pressure or pulse. Occasionally a slight dilatation of the pupil was noted. This was very slight and transient. The urinary output was measured every thirty minutes during a period of two hours. Control patients were observed in the same manner, without the administration of ergotocin. The output in these groups was comparable. A similar experiment was done on a number of women using 2 minims of pituitary extract intravenously. The urinary output was markedly suppressed. The graphs of these experiments show the results quite clearly.

As a result of these observations, we reached the tentative conclusion that the administration of ergotocin in therapeutic doses has little or no effect on the blood pressure curve of patients with or without hyperten-

sion. We also believe that there is no effect on urinary output. Both of these facts are of considerable importance, particularly in dealing with patients manifesting evidence of the various types of toxemia.

We have also noted the possibilities of alterations in pulse rate and respiration in all our patients. There has been practically no change in either the pulse or the respiration rate.

#### CLINICAL OBSERVATIONS

It is, of course, too early to reach any final conclusions relative to all the clinical applications of this recently isolated principle of ergot. We have, however, had some opportunity to observe the effect of ergotocin on various puerperal states. The bulk of our observations pertain to its use during the postpartum period and the third stage of labor. We have had a considerable opportunity to observe its effect upon the uterus exposed through an abdominal incision during the progress of hysterotomy and cesarean section.

We have observed the results obtained in other smaller groups of cases. The beneficent effect of its use in the treatment of abortion, especially incomplete abortions with bleeding, is apparent from a few cases in which we have used it. The administration of 0.25 mg. at four-hour intervals was followed by uterine contractions and the expulsion of retained secundines and a control of the hemorrhage. Most of these patients had no subsequent hemorrhage and required no operative procedure. There are a few interesting observations relative to its use in these cases of abortion. In one patient who gave a history of idiosyncrasy to ergot, there was nausea and vomiting on two occasions following the use of ergotocin. This patient also vomited after the administration of styptieine intramuscularly. In some cases of therapeutic abortion the emptying of the uterus was accompanied by the administration of ergotocin. The uterus could be felt to contract firmly. In one case, in which spinal anesthesia was used, the uterus contracted equally well. This confirms the experimental observations indicating that ergotocin may act through the sympathetic system or directly upon the uterine muscle.

This drug has not been used during the first and second stages of labor. We feel that the same or even greater dangers attend the use of ergotocin during these stages of labor than would accompany the administration of any potent oxytocic drug. We have observed its action during the placental stage of labor in seventy-five cases. These cases are divided into two groups.

First, where the baby was delivered through the normal passages, 0.25 mg. of ergotocin was given intravenously in fifty-one of these cases as the second stage was being completed. The uterine muscle contracted firmly and promptly after

this administration. The placenta separated spontaneously in all of these cases with one exception. Delivery of the placenta was spontaneous after an average duration of a little over four minutes. The maximum time was fourteen minutes and the minimum time was two minutes. In the one exceptional case the patient gave a history of having had a retained placenta followed by manual removal the year previously. In this patient it was necessary to remove the placenta manually one hour and eighteen minutes after the completion of the second stage. The blood loss in these cases was minimal, the average being 100 c.c. with a minimum of 10 c.c. and a maximum of 300 c.c. In all of these cases the uterine response was good with firm contractions and no subsequent bleeding.

In the second group of cases the behavior of the uterus during the third stage of labor was observed at cesarean section. We have, in all, twenty-four of these cases, in which 0.25 mg. of ergotocin was given intravenously as the baby was being delivered through the uterine incision. In all of these cases the uterine muscle contracted firmly, the uterine wall became blanched, its contractions drew the peritoneum into small folds spread over the surface of the uterus. These changes show clearly the marked tetany and contractility of the uterus. The placenta was detached smoothly from the uterine site and was gradually pushed into the incision with partial extrusion which could easily be completed by traction on the cord or by lifting it out manually. This separation was completed in an average time of about two minutes with a minimum lapse of one minute and a maximum of five minutes. Manual separation of the placenta from the uterine wall was unnecessary in any of these cases. The uterine cavity remained dry and the blood loss was minimal during the placental stage. The visualization of the uterus in these cases following intravenous use of ergotocin confirmed nicely our kymographic observations and demonstrated clearly its prompt and powerful effect upon uterine tone and contractility.

We define a postpartum hemorrhage as a condition where 500 c.c. or more of blood loss occurs in a postpartum patient. During this period of study we have had occasion to use ergotocin in seven such patients by the administration of 0.25 mg. intravenously. In all of these cases the uterus has responded actively, the hemorrhage has ceased, there has been no further hemorrhage and the postpartum period has progressed normally. No uterine tamponade has been necessary in any of these cases. The prior administration of pituitary extract and usual management had proved ineffectual in five of these patients. The blood loss was of such an extent that it was necessary subsequently to transfuse three of these cases.

As previously indicated, most of our studies and observations have been upon postpartum patients. We have already described the typical graphs which have been obtained and illustrate the observations made upon over a hundred cases. There have been other patients presenting evidence of subinvolution and uterine infection upon whom the clinical effect of the use of ergotocin has been noted. No kymographic studies have been made upon these patients. There are approximately fifty in this group. There are about fifteen patients who gave evidence of uterine

infection between the fourth and eighth postpartum day. Some of these patients received 0.4 mg. of ergotocin orally for three days, three times a day. Others of them received 0.2 mg. intravenously three times a day. Following the administration there was a primary increase in the lochia, contractions of the uterus were stimulated, the foul odor gradually diminished, the amount of lochia decreased, and the corpus progressively diminished in size. The general status of these patients was improved both subjectively and objectively. The uterus seemed to be well involuted at the time of discharge, which occurred about the tenth day in all of these cases.

The group of cases with subinvolution of the uterus, without evidence of infection, consisted of approximately thirty-five patients. In all of these instances the process of involution seemed to be favored by the use of ergotocin.

We have considered the possibility of using this very potent oxytocic for the purpose of inducing labor. We have been fearful of the dangers which might be incurred because of the powerful contractions and the marked tetany of the uterus which have been noted during the third stage and postpartum period. We have tried it in minimal doses in a few cases without very conclusive results. Somewhat larger and longer continued doses were used in one case where there had already been an intrauterine fetal death prior to its administration. In this case we seemed to secure some results from the attempt at medicinal induction. We are very hesitant about advocating the use of ergotocin for the induction of labor.

#### CONCLUSIONS

We have isolated in crystalline form the active principle of ergot which is responsible for most, if not all, of the desirable oxytocic effect of ergot. We have designated this substance as ergotocin. It is potent in minimal doses by various methods of administration. It does not deteriorate readily and is constant in its action. It is relatively free from untoward or undesirable effects. Its margin of safety is very great as the degree of toxicity is very low. It has no apparent detrimental effect upon respiration, pulse, blood pressure, or urinary output. This emphasizes the value of its use in cases having evidence of cardiovascular renal diseases or toxemias where oxytocic action is required. We are not advocating its use during the third stage of labor, but believe it may be used during this stage as safely and more effectively than any other known oxytocic drug. It is extremely valuable in stimulating uterine contractions in the immediate and remote postabortal and postpartum periods. Its prompt effect in producing tetany and contraction of the uterus, and its prolonged action, make it of special value in the manage-



ment of postpartum hemorrhage. With the isolation of ergotocin the age-old problem concerning the oxytocic principle in ergot apparently has been brought to a close. We now have all the desirable, potent, oxytocic activity in ergot isolated in a crystalline material, stable, and nontoxic. Ergotocin can be used safely whenever oxytocic therapy is indicated.

#### REFERENCES

- (1) Davis, Adair, Rogers, Kharasch, and Legault: *AM. J. OBST. & GYNEC.* 29: 155, 1935. (2) Davis, Adair, Chen, and Swanson: *J. Pharmacol. & Exper. Therap.* 54: 398, 1935. (3) Moir: *Brit. M. J.* 1: 1119, 1932. (4) Adair and Davis: *AM. J. OBST. & GYNEC.* 27: 385, 1934. (5) Kharasch and Legault: *Science* 81: 388, 1935. (6) Kharasch and Legault: *J. Am. Chem. Soc.*, June, 1935. (7) Dudley and Moir: *Brit. M. J.* 1: 520, 1935. (8) Koff: *Surg. Gynec. Obst.* 60: 190, 1935. (9) Broom and Clark: *J. Pharmacol. & Exper. Therap.* 22: 59, 1923. (10) Henry, Thomas Anderson: *The Plant Alkaloids*, Philadelphia, 1913, P. Blakiston's Son & Co.

### THECA CELL TUMORS

SAMUEL H. GEIST, M.D., NEW YORK, N. Y.

(From the Gynecological Service and Laboratories of Mt. Sinai Hospital)

A UNIVERSALLY accepted classification of ovarian tumors has not been presented as yet. The recent advances in our knowledge of these neoplasms has been based on our better understanding of the embryologic development of the ovary and on our realization that the gonadal hormones and their clinical manifestations may prove important factors in identifying tumor types.

In the early embryo the epithelial covering of the gonadal anlage becomes many layered and invades the underlying mesenchyme in the form of cords (Fig. 1). The cells in these cords later form the true parenchyma of the gonad. This so-called indifferent stage rapidly evolves into the definitive gonad, and the fate of the original invading cords vary with the type of gonad (male or female) that develops. In the male these cords form the tubular system of the testicle and possibly the interstitial cells. In the female these cell cords give rise to the forerunners of the granulosa cells and the theca interna cells.

Fischel and recently Schiller have suggested that these parenchymal cells of the ovary are the results of a transformation in situ of the mesenchymal tissue and though they have the properties of epithelial cells they are not really derived from the gonadal surface epithelium. Irrespective of which origin is accepted, the fact remains that in the ovary two cell types exist in the ovarian parenchyma, granulosa cell forerunners and theca cell forerunners destined to ripen in the later development of the gonad into mature granulosa and theca cells.

The parenchymal cells, both granulosa and theca interna, have definite common characteristics. They both store or form lipoid, and they both store or produce an estrogenic hormone. Zondek showed that the theca interna cells contain an estrogenic hormone in greater amount than in the granulosa. The lipoid also differs in the two types of cells; in the granulosa it is scant in amount, being found in quantity only when the cells are undergoing degeneration, while in the theca cells it is much greater in quantity in the normal functioning cell. In addition, in the granulosa layer it is mainly phospholipid whereas in the theca it is mainly cholesterol or the esters.

Both types of cells have an influence on connective tissue growth, apparently stimulating it to develop. This connective tissue has a tendency to hyalinize. This stimulating effect on the connective tissue

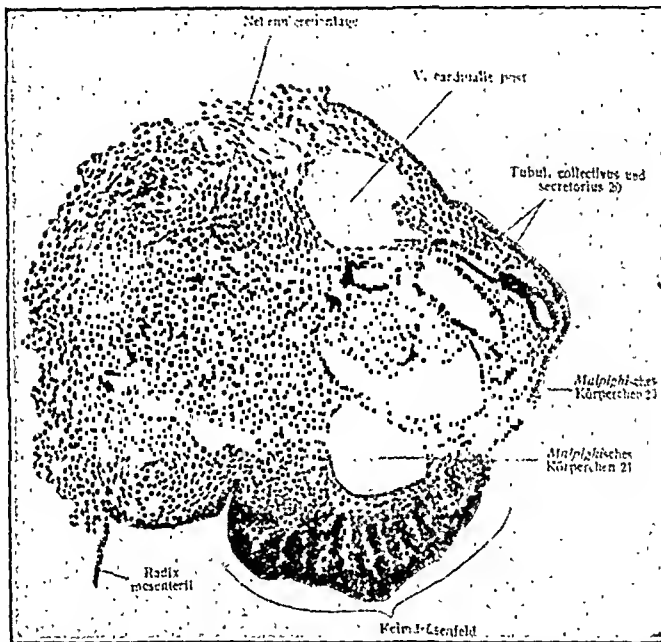


Fig. 1.—Illustrating invasion or mutation of mesenchyme into epithelial cords.

also seems a more marked characteristic of the theca cells. It has also been suggested by Löffler and Priesel and others, that the theca cells even may produce fine connective tissue fibrils a property that Schiller has emphasized as substantiating the mesenchymal origin of these cells.

It is natural to suppose that these immature granulosa cells and theca cells may give rise to tumors. R. Meyer and others have described tumors, termed by V. Werdt granulosa cell tumors, which have been accepted as having their origin from these unripe granulosa cells of the parenchyma.

Löffler and Priesel in two publications have reported ten cases, and Melnick and Kanter have added two additional cases that because of very definite gross and histological characteristics, they believed arose from the theca cells of the ovarian parenchyma.

We have been able to assemble five tumors which we believe fall into this group. In the ten cases reported by Löffler and Priesel, two occurred before the menopause. One in a young woman of eighteen the other in a mature woman of thirty-seven. The two cases reported by Melnick and Kanter, both developed after the menopause and in our group of five cases one occurred in a young woman of twenty-one years of age.

The following are the cases studied with the available clinical data. In view of the fact that three of the five were old cases and the specimens found in our collection of tumors, the clinical data were scanty and chemical and hormonal studies could not be undertaken.

CASE 1.—(Courtesy of Dr. Neuhof) R. M. was a married woman, aged forty-eight years. Her previous history was negative. The menstrual history was normal,



Fig. 2.—Case 1, showing large striated tumor, grossly yellowish white, in close association with dermoid cyst. Woman forty-eight years of age, no bleeding.

and there were no evidences of endocrine disorder. The physical examination revealed a ballotable tumor, apparently attached to the right adnexa, the size of a child's head. At operation the tumor was removed leaving the grossly normal uterus and left adnexa. The patient made an uneventful convalescence.

The specimen was composed of two distinct masses (Fig. 2), one a nodular oval tumor, hard yellowish white and encapsulated. This measured 18 by 15 by 10 cm. The second portion was a typical dermoid closely applied to the solid tumor but apparently not a part of it.

The solid tumor on section presented a gross appearance corresponding to some of the specimens described by Löffler and Priesel, and Melnick and Kanter. It showed small light yellow areas separated by septa of white connective tissue more or less uniformly distributed over the entire surface. The yellow areas varied from 0.5 to 1.5 cm. in diameter. The connective tissue septa varying in width from very fine strands to thickened bundles 5 to 7 mm. wide.

Histologically the yellow areas were composed of masses of elongated oval cells with blunt ends, or of polygonal cells with a vesicular or at times a deep staining

nucleus surrounded by a faintly staining vacuolated protoplasm. In some of the cellular islands the cells appeared as masses of spindle cells, suggesting a spindle cell sarcoma (Fig. 3). Fat stains demonstrated that these cells contained lipoid masses of varying size (Fig. 4). The globules are found mainly in the cells but appear to some slight extent in the interstitial tissue. The globules are doubly refractile.

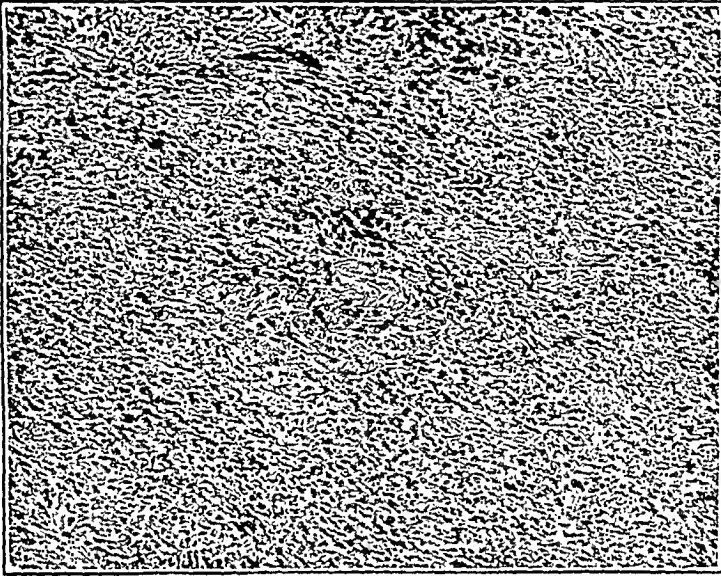


Fig. 3.—Masses of small, plump spindle cells suggesting sarcoma.

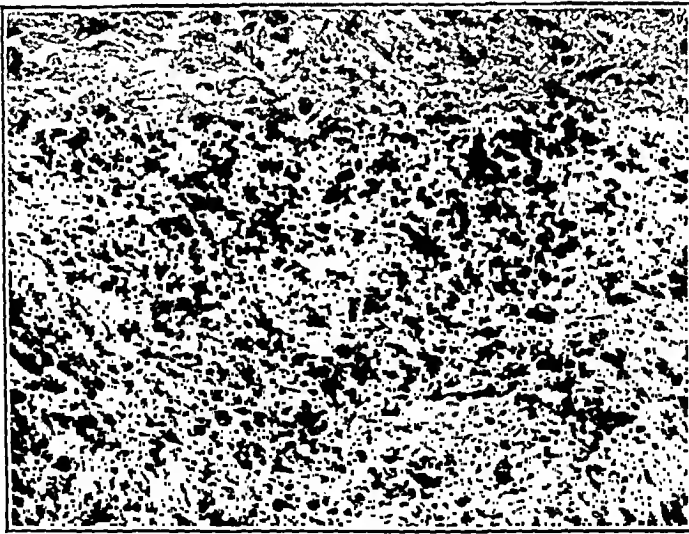


Fig. 4.—Graph obtained after the intramuscular administration of 0.4 mg. ergo-

In the cellular islands are found hyaline plaques (Fig. 5) of connective tissue surrounded by the spindle cells. Fine fibrils extend out from these hyaline plaques to separate the cells into small groups or even into isolated units. In some areas the connective tissue fibrils seem to enter or emerge from the spindle-like epithelioid cells.

The white septa are connective tissue bundles containing few cells. In the meshes of the bundles are found the remains of large polygonal epithelioid cells,

which cells also contain fat. The bundles are composed of fine fibrils possibly the products of the cells above described or the result of the stimulation by these cells of the intercellular substance. These fine fibrils may extend between the individual cells. There is a marked tendency for this tissue to undergo a hyaline change which can be especially well seen in the connective tissue islands already described.

The cellular areas were vascular, the vessels being both thin and thick walled and occasionally dilated. Pigment containing cells were found in the cellular areas (probably lipochrome) and occasionally in the vessel endothelium.

The tumor had been fixed before the nature of the growth had been determined so that hormone studies were not undertaken. However, a chemical estimation of the lipoids was made by Dr. Gerhard Rosenthal. The material was treated according to the method of Sabottka, Epstein and Lichtenstein.<sup>1</sup> The tissue was finely chopped and extracted for several weeks with cold acetone. After the evaporation the residue was extracted with hot alcohol. It is presumed that in this fraction all the neutral fat as well as a certain proportion of the phospholipoids are contained. A second extraction of the chopped residue, left after the cold acetone and hot

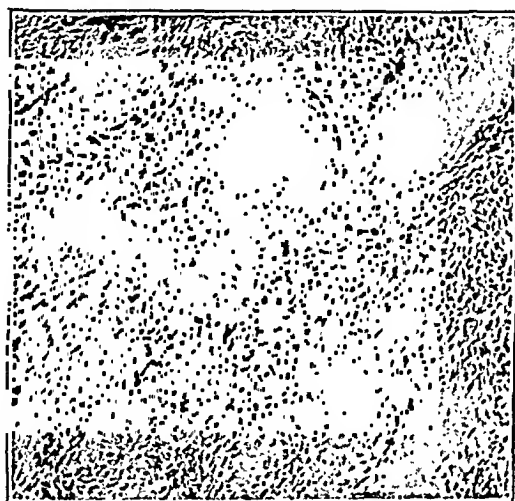


Fig. 5.—Hyaline plaques in cellular areas with fine connective tissue fibrils.

alcohol extraction, was made with hot acetone in the Soxhlet apparatus. This was extracted subsequently with ether and thus most of the lecithin (cephalin) and cerebroside were obtained. Finally extraction with hot alcohol to obtain the remaining cerebroside and sphingomyelides was completed. Cholesterol and cholesterol esters were determined according to Bloor, phosphorus according to Kuttner and Cohen, and nitrogen by the micro Kjeldahl method (Table I).

The following is a résumé of the findings. The weight of the fresh material was 109 gm. The total lipid extract was 2.99 gm. -2.7 per cent of the fresh material. All the weights in the table are in grams per cent of fresh material. The total phospholipoids of all three extracts amount to 0.352 gm. or 0.321 per cent of the fresh material.

The cholesterol and cholesterol esters to 1.180 gm. or 1.1 per cent. These figures show that we are dealing with a tissue of comparatively little lipid content, of which the cholesterol fraction is very high in relation to the other lipids, as well as to the fresh material. This is easily understood when one realizes that the bulk of the tumor is fat-free connective tissue. It has also been noted that the fat in

the cells is double refractile. Only about one-fifth is free cholesterol, the other part is esterified. The blood cholesterol and esters were studied and normal figures were obtained. Total cholesterol in the blood was 140 mg. Total cholesterol esters in the blood were 31 mg. In other words, the cells of the neoplasm either store or form cholesterol and cholesterol esters. The process is not due to a metabolic disturbance as evidenced by the normal blood figures.

TABLE I\*

GRAMS OF EXTRACT	TOTAL CHOLESTEROL	CHOLESTEROL OF THE ESTER	FREE CHOLESTEROL	CHOLESTEROL ESTER	PHOSPHORUS	PHOSPHOLIPIDS	BALANCE NEUTRAL FATS AND CEREBROSIDES
ACETONE EXTRACT (NEUTRAL FAT SOME LECITHIN)	0.746= 684 mg. %	1.630= 578 mg. %	0.116= 106 mg. %	1.06= 972 mg. %	0.012= 11 mg. %	0.312= 286 mg. %	1.268= 1.1 mg. %
ETHER EXTRACT (MOST LECITHIN 0.01 SOME CEPHALIN)	0	0	0	0	0.00056 =0.51 mg. %	0.015= 14 mg. %	0
ALCOHOL EXTRACT 0.22 (CEREBROSIDES SPHINGOMYELIDES)	0	0	0	0	0.00096 =0.88 mg. %	0.025= 23 mg. %	0.195= 180 mg. %

\*All weight in grams-percentage of fresh material.

CASE 2.—G. H. was a patient on the Gynecological Service at Mount Sinai Hospital. She was twenty-one years old, had been married four years and never had been gravid. Her menses began at the age of eleven and up to her sixteenth year were regular and normal. From the sixteenth to the seventeenth year she had bled daily. Since her seventeenth year she had bled every other week, the periods lasting from five to six days. For four months she bled daily except for the past month during which time there had been no bleeding. She had also noted a definite enlargement of both breasts. The physical examination revealed the presence of a left-sided firm pelvic mass, the size of an orange, and a moderate hypertrophy of the breasts. At operation a left salpingo-oophorectomy was done removing a firm oval ovarian tumor with slightly irregular surface about the size of a tangerine (Fig. 6). On section it presented a yellowish color due to small islands of yellow tissue separated by connective tissue bundles resembling somewhat the tumor in Case 1. In addition small hemorrhages were present and several small cysts and one large one about 2 cm. in diameter were found.

The other ovary was normal, the uterus was soft, succulent but otherwise normal.

In the main the histologic findings resembled those described in Case 1. However, there was a tendency for the fibrous tissue to preponderate and the epithelioid cells were more vacuolated (Fig. 7).

Hormone studies were made of the tumor tissue by Dr. F. Spielman. The fluid from the cyst was examined but as only a small amount was available, conclusions cannot be definitely drawn. In amounts up to 0.5 c.c. the fluid did not contain one mouse unit of estrogenic hormone. However, in view of the fact that these cysts are degenerative in origin this finding is not unlooked for.

The tumor tissue itself when extracted showed the presence of one mouse unit per 0.75 gm. of tumor tissue, an amount greater than that found in the placenta. This finding seems to show that these tumors may either produce or store an estrogenic hormone and suggests that the cells of the tumor have some epithelial characteristics.

Since the operative removal of the tumor, the periods have returned to normal occurring every twenty-eight days. The patient now has had six normal four-day periods. Her breasts have grown smaller. This case is to be published in the *Journal of the American Medical Association*.

CASE 3.—(Courtesy of Dr. A. A. Berg.) H. C., a woman sixty-five years of age had an uneventful menopause fourteen years ago. For the past six years she noted an abdominal mass. For the past month she has noticed painless, odorless vaginal bleeding. The physical examination was negative except for the presence



Fig. 6.—Case 2. Firm yellowish, white tumor with numerous degenerated cysts, twenty-one years old. Atypical bleeding, breasts enlarged, estrogenic hormone present.

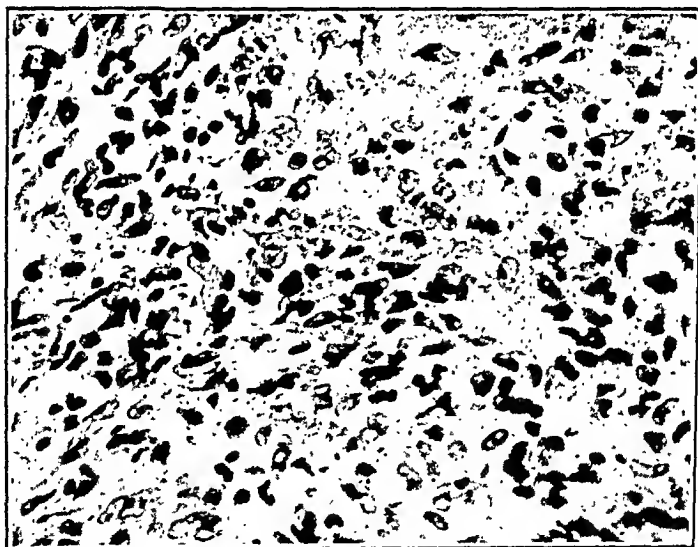


Fig. 7.—Cellular areas with connective tissue, vacuolated fat containing cells.

of a large hard nodular tumor, about the size of an adult's head, filling the lower abdomen. The vaginal examination did not disclose the origin of the tumor. There was no ascites. At operation, a solid tumor of the right ovary was removed. The uterus and left adnexa were left in situ. There was no observation relative to the condition of the uterus, its size or succulence.

The specimen grossly is a nodular tumor measuring 11 by 7 by 6 cm. The surface is smooth and the consistency uniformly hard. A fibrous capsule surrounds

the growth. It cuts with difficulty, like a fibroma durum, and on section presents a striking appearance. In different areas of the tumor, mainly peripheral, are well demarcated yellowish areas of varying size from 2 cm. to 6 cm. in diameter. On close scrutiny these areas present small white glistening bands radiating from numerous points in the yellow areas (Fig. 8).

Occupying a large part of the tumor, about one half the total area, is a broad surface densely hard and almost pure white. It is striated and here and there a faint yellowish island of tissue can be identified.

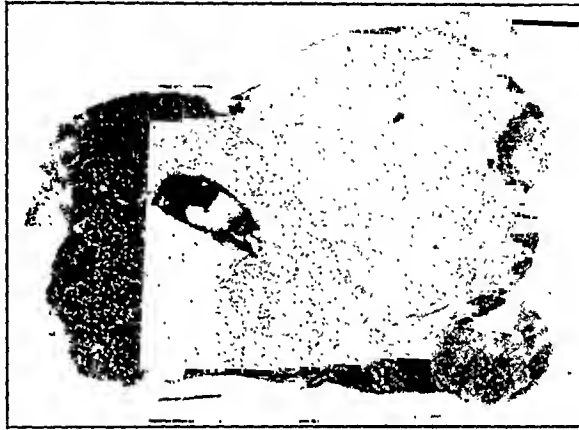


Fig. 8.—Case 3, sixty-five years old. Vaginal bleeding, densely hard tumor showing discrete yellow nodules and massive hyaline connective tissue development.



Fig. 9.—Hyaline tissue with few connective tissue cells from dense area of tumor.

The gross appearance of the tumor is so peculiar that one immediately realizes that it is an unusual neoplasm probably desmoid in character. The fibrous nature of the growth is most striking.

On histological study two main elements stand out that aid in identifying the tumor. One is the marked production of connective tissue with a tendency to hyalinization or collagenous change (Fig. 9) and the second is the large masses of fat-containing epithelial cells that are present (Fig. 10). The yellow areas that were grossly conspicuous are composed of large spindle cells with blunted ends and



large oval centrally placed nuclei at times vesicular, at others darkly stained with a definite nucleolus. The cytoplasm is somewhat vacuolated and Sudan stains show these vacuoles to be fat globules. They vary in size, and while most of them are intracellular, globules are found between the cells.

The fibers run in bundles, which cross each other in no definite order, suggesting the interlacing arrangement of a cellular fibroma or fibromyoma. Often in the

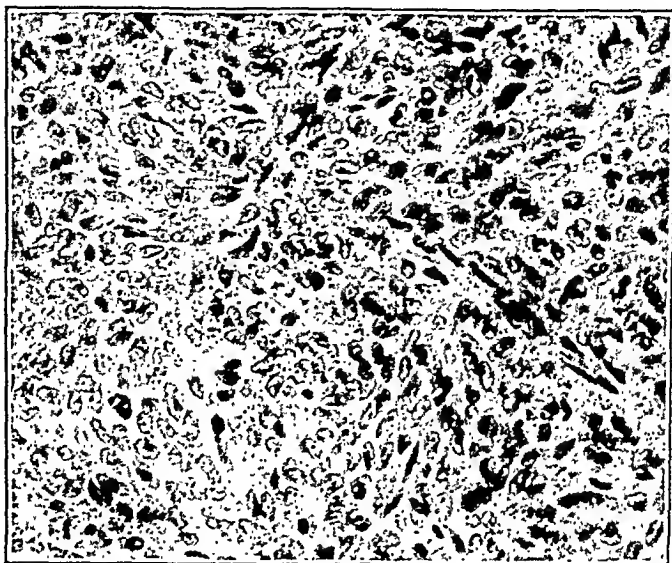


Fig. 10.—Spindle polygonal cells from yellow areas. These were fat containing cells.



Fig. 11.—Massive fibrous tissue. Surrounding and compressing epithelial cells. These cells still contain fat.

midst of the cellular areas small islands of fibrous tissue can be found, and in addition bands of fibrous tissue are seen extending into the cellular areas. Close study of the cells in this region, by means of special stains, as Mallory, Van Gieson, and Bielechowsky, indicates that the connective tissue fibrils are closely associated with the epithelial cells, and not a replacement phenomenon due to degeneration. Fine fibrils seem to reach out from the cells, which fibrils surround the cells, fuse into larger, coarser strands and bundles, and then merge to form the collagenous islands

that contain the shadowy outline of a few cells or an occasional pale staining nucleus (Fig. 11). In these fibrous areas fat is found only in scanty amount. At the periphery of such a plaque, the fat is more prominent and in larger amounts. Löffler and Priesel have given an excellent description of the relation of the connective tissue to the epithelial cells and have expressed the opinion that this tissue is a product of the cells.

In the dense white areas the histological study demonstrates the structure to be almost entirely connective tissue showing collagenous areas. Here cells are very scanty in amount and fat is practically absent.

One gets the impression that the cells that compose the tumor have the function of accumulating lipid material, and also of producing connective tissue or stimulating its growth. When the one function is in the ascendancy the other practically ceases. Blood vessels are numerous, especially in the cellular areas, where they are dilated, while in the connective tissue zone they are rare. Occasionally pigment is present in the endothelial cells of the vessels and in some of the fusiform cells. This is lipoid pigment that has accumulated in the cells.



Fig. 12.—Case 4, fifty-nine years of age. Vaginal bleeding, thick wall cyst, bright yellow color, inner wall shaggy, contains blood.

CASE 4.—(Courtesy of Dr. A. A. Berg.) D. R., the patient was fifty-nine years of age, married and had three children. She had had a normal menopause seven years before and was admitted to the hospital with a history of severe lower abdominal pain and vaginal bleeding. There was a history of previous abdominal pain but no bleeding. The physical examination was negative except for the presence of the large tender fixed abdominal mass which by vaginal examination was diagnosed as a twisted right ovarian cyst. At operation a twisted hemorrhagic, right-aided, thick-walled ovarian cyst was removed. The uterus and left adnexa were left in situ. There was no observation noted relative to the size or condition of the uterus.

The specimen received in the laboratory was a collapsed thick-walled cyst, the wall measuring 1.5 cm. in thickness and of a bright yellow color (Fig. 12). The appearance of the wall was that of a tiger skin except that instead of a yellow and black striping it was yellow and white. In some areas the evidences of torsion were noted in the wall. The inner wall was shaggy in places, but no papillae were present. The original diagnosis was a twisted, fibro-xanthomatous cyst. However,

on further study, the wall showed the typical appearance of cellular islands composed of large fusiform and polyhedral cells with vacuolated protoplasm and containing lipid. The connective tissue strands resembled those in the tumors already described. The tumor had been fixed in formalin and so hormone studies were not undertaken.

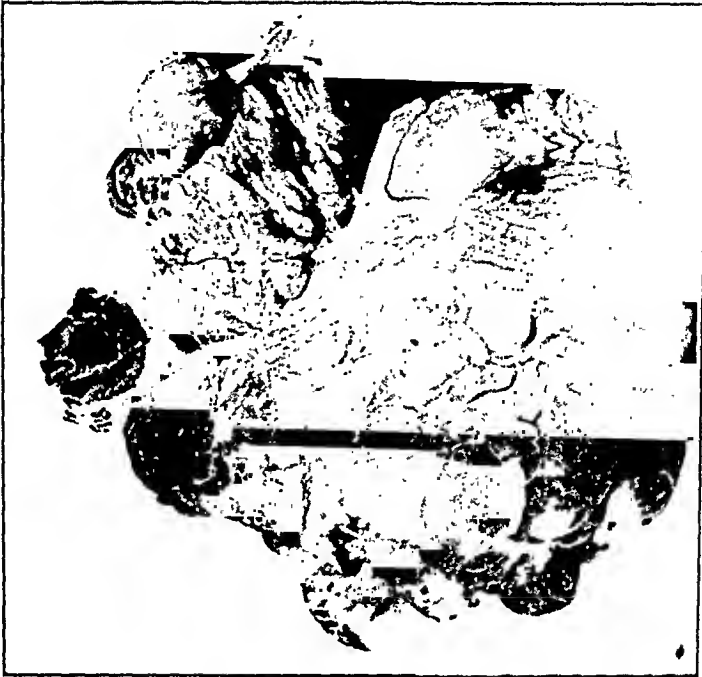


Fig. 13.—Case 5, sixty-five years old. No vaginal bleeding, multilocular serous cyst adenoma with densely hard yellowish white solid tumor near the center.



Fig. 14.



Fig. 15.

Fig. 14.—Showing connective tissue arrangement with fine fibrils extending into the cellular islands surrounding individual cells.

Fig. 15.—Fat stain showing distribution of fat in cellular islands.

CASE 5.—(Courtesy of Dr. A. A. Berg.) S. G. was a woman, sixty-five years of age. Her previous history was irrelevant. She had had a natural menopause fifteen years ago and there had been no further vaginal bleeding. Recently she had noticed a gradual enlargement of the abdomen and some edema of the legs.

The physical examination was negative except for the presence of a large abdominal mass reaching almost to the ensiform. There was some edema of the legs. She had evidence of a chronic nephritis. A diagnosis of an ovarian cyst was made and at operation a large cystic tumor of the left ovary was removed with the slightly enlarged uterus and right tube.

Grossly the specimen consisted of a uterus and left ovarian mass. The uterus was slightly larger than normal in size, the endometrium pale, thickened, granular and from the left cornu a polyp 2 cm. in length projected. The ovarian mass consisted of numerous grapelike large cysts, smooth, bluish in color and at one point a solid mass 5 cm. in diameter was present (Fig. 13). The solid tumor presented



Fig. 16.—Hyperplastic endometrium, associated with theca cell tumor in a woman sixty-five years of age (Case 5).

a yellowish white color with pearly white septa traversing its cut surface. There were also a number of small cavities at one pole. The cysts were thick walled and contained a thick yellowish green mucoid material. In two of the larger cysts small granular hemorrhagic excrescences were found.

The histologic examination demonstrated that the cysts were typical multilocular, benign serous cysts.

The solid tumor was made up of cellular islands composed of plump spindle cells separated by connective tissue bands and masses. The connective tissue fibrils in places extending into these islands and separating the individual cells (Fig. 14). There was a definite tendency for the connective tissue to be hyalinized and small plaques could be found.

The cellular islands contained a large amount of double refractile fat globules and only a very scanty amount was present in the connective tissue (Fig. 15). The uterine mucosa histologically was hypertrophic (Fig. 16), and the polyp presented the same histological pattern.

## DISCUSSION

The published cases of Löffler and Priesel, of Mehnick and Kanter and of our own permit us I believe to classify this group of tumors as a definite clinical and pathological entity.

Clinically these tumors are unilateral neoplasms occurring commonly after the menopause. In three cases of the seventeen they occurred before the menopause, two published by Löffler and Priesel, and one of our cases.

Aside from the symptoms of any pelvic neoplasm these tumors present in most instances a definite and clear-cut syndrome. The most striking symptom is atypical bleeding, usually postmenopausal as this is the common age of tumor occurrence.

In one of our patients twenty-one years old there had been a history of bleeding for a year with a short period of amenorrhea following the bleeding. In a case of Löffler and Priesel, aged eighteen, a similar history was obtained. In addition one patient noted an enlargement of the breasts. The uterus was enlarged and soft and in the cases where the endometrium was examined it was found hyperplastic. Endometrial polyps were found in several cases. After the removal of the tumors the symptoms regressed.

While in one instance Löffler and Priesel report a case as malignant all the others thus far observed apparently have remained well after operation.

The gross and histologic appearance is most striking and characteristic. The tumors are hard, somewhat nodular growths that may reach the size of an adult's head. They suggest a fibroma in consistency and appearance, but unlike fibromas are not accompanied by ascites. Löffler and Priesel report one case with 250 c.c. of ascitic fluid. However, the tumor may be represented by a large degenerated cystic mass as in one of our own cases (Case 4), previously diagnosed a twisted fibroxanthoma, or may be associated with other growths as Case 1 with a dermoid and in Case 5 with multilocular serous cysts. On section the cut surface is distinctive. The color is usually yellowish white, this being due to the presence of varying sized yellow cellular islands separated by finer or coarser hyaline connective tissue bundles. The connective tissue may be so massive in amount that the cut surface of the tumor may exhibit white hyaline areas containing only tiny pinhead sized islands of light yellow color, and in addition may be studded with a few or many larger isolated nodules of deep yellow tissue surrounded by the hyaline masses. Small hemorrhagic areas are found and at times small sized cysts that may reach the diameter of a walnut. These cysts may coalesce and form larger cysts.

Histologically these tumors present a characteristic picture. The yellow areas are composed of plump spindle or polygonal cells with

a central or at times an excentric elongated or irregular nucleus, dark staining and rich in chromatin. The cells have an epithelioid appearance. The cell protoplasm is vacuolated and contains fat (Figs. 4, 17, and 15). The fat globules may also be present in the interstitial tissue to some slight extent but only when cells are still present. The fat then is usually found at the periphery of the connective tissue plaques and strands and these fat globules are very tiny in contradistinction to the large globules and masses in the cells. Pigment granules are occasionally present in the epithelioid cells. Blood vessels are present but not in great number. They appear both as fine capillaries and as large vessels. They are found in the connective tissue capsule and at the periphery of the cellular islands. The vessel endothelium contains pigment granules (lipochrome).

The connective tissue bundles are hyaline to a great extent, and often large hyaline plaques are present in the midst of a cellular island with fibers extending out radially and surrounding the individual cells or seeming to enter them.

The fibrous tissue bundles vary in size, density, and structure. They may be very fine, composed of but a few fibrils or so massive as to represent the greater part of the tumor. They may be composed of a few connective tissue bundles or large masses of hyaline tissue. Connective tissue cells are usually scanty in number and in some of the fibrillar meshes isolated cells resembling the true tumor cells and containing fat are found. The connective tissue bundles run in a criss cross net work surrounding the cellular areas. Finer fibrils may encircle cell groups or even individual cells. It seems that where the connective tissue is actively proliferating it throttles the growth of the epithelioid cells.

The cysts as previously mentioned are probably degenerative in origin. The walls may be smooth or as in the large one previously described shaggy. The contents are a yellowish clear or turbid fluid containing cholesterol crystals, fat droplets and cellular debris. There is no definite lining though occasionally a flattened endothelial-like row of cells is found in scattered areas.

In addition to the characteristic clinical and pathological picture above described these tumors present other definite features. The chemical study as well as the microchemical and polariscopic investigation demonstrates that these tumors contain fat. The fat to a great extent is cholesterol and cholesterolester and not degenerative in nature. It is limited almost entirely to the cellular elements comprising the tumor and is found only in tiny scattered globules in the connective tissue. In the granulosa cells as pointed out by Melnick and Kanter the fat is usually phospholipid, while here the greatest amount of lipoid was in the nature of cholesterol and cholesterolesters.

Melnick and Kanter suggested on purely hypothetical grounds the possibility that these tumors were able to produce an estrogenic hormone. Dr. Frank Spielman examined one such tumor for its estrogenic hormone content and found that the tumor contained one mouse unit per 0.75 gm. of tissue extracted. This demonstrates that these tumors can produce or store an estrogenic hormone. The investigation of various other solid and cystic tumors of the ovaries failed to demonstrate the presence of an estrogenic hormone except in follicular cysts as demonstrated by Robert T. Frank, and in the granulosa cell tumors as shown by Salmon by extraction and by R. Meyer and others by implantation. It has been found in uterine tumors and other tissues in small amounts.

To recapitulate: We have described a group of five tumors that have definite clinical, pathologic, hormonal and chemical characteristics. They are differentiated from fibromas or fibrosarcomas by the mottled yellow appearance due to the cellular islands separated by connective tissue and the absence of ascites. Apparently the growth is the product of a cell type that has the potentiality of not only reproducing its type but of forming connective tissue fibrils or stimulating the intercellular substance to become fibrillar.

The removal of the tumor causes a cessation of the clinical signs and a regression of the abnormal findings. This suggests that the hormone content may play a rôle in producing the signs and symptoms of the disease.

The theca interna cells of the ovarian parenchyma can produce or store an estrogenic hormone, and can produce or store lipid. They also stimulate the formation of connective tissue which has a tendency to hyalinization as noted in the regressive follicle or corpus atreticum.

While the granulosa cells to a certain extent have similar properties there are sufficient points of difference to enable us to separate the granulosa cell tumors from the theca cell tumors.

The gross appearance of the two tumor types is distinctly different, the theca cell tumor being a hard, fibrous yellow growth whereas the granulosa cell tumor is a more cellular, medullary, softer neoplasm. Nowhere in the theca cell tumors does one find areas suggestive of the morphology or pattern of the granulosa cell tumor. The former is a much more uniform tumor. The lipid distribution in the granulosa cell tumors differs from that in the theca cell tumor.

The clinical symptoms are similar, but with cells having such closely allied biological properties it is but natural to expect the same clinical picture. In none of the seventeen cases do we find the tumor in children whereas Klaften has reported that 8.9 per cent of granulosa cell tumors occur before puberty. Furthermore while granulosa cell tumors occur in 48.8 per cent after the menopause in this group of seventeen cases 83 per cent occurred postmenopausal.

Because of the histologic, chemical and biological resemblance of these tumor cells to the theca interna cells of the ovarian parenchyme it is suggested that the theca interna cell forerunners in the ovary are histogenetically involved.

## REFERENCES

- Fischel, A.*: Ztschr. f. Anat. 92: 34, 1930. *Frank, R. T.*: J. A. M. A. 78: 181, 1922. *Geist and Spielman*: J. A. M. A. 104: 2173, 1935. *Löffler and Priesel*: Beitr. z. Path. Anat. u. Allg. Path. 90: 199, 1932; Wien. med. Wchnschr. 84: 400, 1934. *Melnick and Kanter*: AM. J. OBST. & GYNEC. 27: 41, 1934. *Schiller*: Path. u. Klinik. der Granulosa zellentumoren, Wien, Maudrich, 1934. *Werdt, F.*: Beitr. z. Path. Anat. 59: 453, 1914. *Zondek*: Die Hormone des Ovariums und des Hypophysen Vorderlappens, Berlin, 1931. *Sobottka, Epstein, and Lichtenstein*: Arch. f. Path. 10: 677, 1930. *Kuttner and Cohen*: J. Biol. Chem. 575: 516, 1927.

100 EAST SEVENTY-FOURTH STREET

## SOME NEWER ASPECTS OF REPRODUCTIVE PHYSIOLOGY

EMIL NOVAK, M.D., BALTIMORE, MD.

(From the Gynecological Department, Johns Hopkins Medical School)

IT IS not the purpose of this paper to present a review of recent advances in the field of reproductive physiology, but simply to discuss a few, chosen because of their newness, their importance, and their bearing upon clinical problems. The paper thus deals with trends rather than with individual studies. The literature of reproductive physiology is vast and widely scattered. Many of the most important publications appear in nonclinical journals, so that their contents only slowly reach the current of gynecologic literature. No one person can possibly view the entire changing panorama in the intensively worked field of endocrinology, while the average busy clinician is likely to be so bewildered that he dismisses it all as a hopeless muddle.

It would seem, therefore, that there is a genuine justification for papers which aim at summarizing, simplifying and appraising the rapidly growing knowledge in this general subject, which is so full of potentialities in its application to our clinical problems in gynecology. We would be very short sighted if we allowed our interest to lag merely because thus far so little has been accomplished in the application of reproductive endocrinology to our many problems of treatment of functional diseases in women. In the present state of our knowledge, I personally am far more interested in endocrinology than in organotherapy. To assume the "practical" futility of the former would be just as foolish as to deny the usefulness of a knowledge of the pathology, life history, and general characteristics of such a disease as cancer, just because we do not as yet have a very satisfactory treatment for it.



For this discussion I have selected four subjects which impress me as being timely, important, and perhaps not quite so familiar to most clinicians as they should be. They are (1) the newer studies on the chemistry of the sex hormones; (2) the possible participation of the posterior lobe and the parahypophyseal portions of the midbrain in the reproductive cycle; (3) the question of so-called anovulatory menstruation; and (4) the endocrine factors in menstrual bleeding.

A host of other topics invite discussion. For example, it would be of interest to say a word concerning the bedeviling new concept of anti-hormones, but this is still so nebulous and so unconfirmed that no worthwhile conclusions can as yet be drawn. Again, it might be of interest to include a discussion of the newer work on the physiology of lactation, the elucidation of which is almost entirely due to the work of American investigators, and also the newer developments concerning the effects, normal and abnormal, of the ovarian hormones upon the mammary gland. But considerations of space necessitate selectiveness, and only the few subjects indicated above will be considered in this paper.

#### THE CHEMISTRY OF THE SEX HORMONES

To my mind, the most outstanding development in the field of reproductive physiology during the past few years has been the recent work on the chemistry of the sex hormones, and especially the demonstration of the close kinship in the molecular structure of the male sex hormone, the follicular hormone and progesterin, as well as the remarkable relationship of all three of these to the well-known sterol group of chemical compounds, to the bile acids, to certain vitamins, and to various carcinogenic substances. When one considers that only a few years have elapsed since the discovery (1927), by Aschheim, that estrin is present in large amounts in urine of pregnancy, and that up to the opening up of this large source, chemical studies of the hormone on any large scale had hardly been possible, one can appreciate the rapidity with which our knowledge has been advanced since then. Within a few years estrin was obtained in crystalline form by Doisy and his coworkers, the crystals being for the first time exhibited by Doisy at the International Congress on Physiology, held at Boston in August of 1929. At about the same time, and quite independently, a similar accomplishment was achieved by Butenandt, whose publication appeared a little before that of the American workers. Still other investigators reported similar results almost immediately afterward, indicating what a hot trail all had been following.

It soon became apparent that not all of these studies had yielded exactly the same substance, but that estrin existed in a variety of forms, so that soon it became necessary to distinguish between ketohydroxyestrin ( $C_{18}H_{22}O_2$ ) and trihydroxyestrin ( $C_{18}H_{24}O_3$ ). The former is the

substance isolated by Doisy, and also by Butenandt, while to Marrian is due the credit of isolating the latter. Both occur in the urine of pregnancy, but ketohydroxyestrin is a far more potent physiologic substance than is the trihydroxyestrin. There are various other differences between the two, as regards methods of extraction, solubility and so on, but these need not be discussed here, especially as the present writer makes no pretense to the chemical knowledge necessary to do this intelligently.

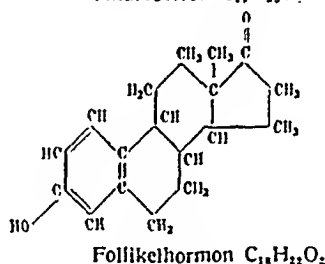
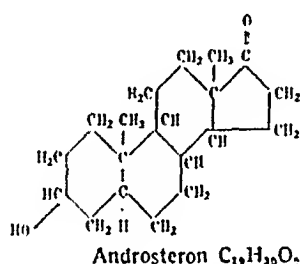
There are still other forms of estrin described (the alpha, beta and delta forms, equilin, hippulin, etc.), while almost nothing is known of its fate in the body. It has even been suggested that the estrin found in the urine of pregnancy is not identical with the estrin produced by the ovaries. There are many other unknown factors, such as our uncertainty as to how much estrin is produced in the body, how much is taken in with food, how and in what chemical form it is utilized by the organs, and how much of it is destroyed and where, so that really we can determine only how much is eliminated. Even this, as Siebke emphasizes, is inaccurate, for such determinations deal with definite amounts obtained by one technic or another, with no certainty that this reflects the amount of original hormone present in the blood, and perhaps not indicated by the technic employed. We do not know whether all of the variants of estrin are essential for the female cycle, or whether they represent only excretion derivatives. This confuses blood and urine hormone studies a great deal, especially as there is the widest variation in the potency of the various forms of estrin. For example, as Schoeller says, if  $\alpha$  (alpha) folliculin is excreted as the hydrate, with a drop in potency from 8 or 10 million mouse units to 75,000 units per gram, it can be seen that interpretations based on the urine hormone output would necessarily be very erroneous.

As regards the chemistry of the corpus luteum hormone (progesterin), there has been the same intensive pursuit of its structural formula, the pioneers being Allen, Butenandt, and Slotta, Rusehig and Fels. Butenandt gives its chemical formula as  $C_{21} H_{30} O_2$ , and he, with Westphal and Hohlweg, in April of 1934, described the preparation of a crystalline chemically pure substance with this formula. Here again there are a group of closely related substances to be dealt with.

My purpose in discussing the chemistry of these hormones, however, is to emphasize, first, a fact which may prove to be of great clinical importance, viz., the close structural relation which exists between the two ovarian hormones and between them and the male sex hormone, androsterone or androsteron. This is at once evident from the fact that all three of these hormones are built up around the same phenanthrene group, composed of 3 six-membered rings. Phenanthrene itself, rather curiously, is quite inactive, but the various sex hormone derivatives possess various types and degrees of physiologic potency.

Long before these fundamentally important facts had been established, it seemed logical to believe that there must be some very close relationship between estrin and progestin, for both are products of essentially the same cell. Just as the lutein cell is only a modified granulosa cell, so it seemed that progestin would prove to be only a modified estrin. This, indeed, is what actually seems to be the case.

Just as surprising as the relation between estrin and progestin is that which exists between the male and female sex hormones. It has long been known that estrin is at times found in the urine of men, and the male hormone in the urine of women. As a matter of fact, perhaps the most surprising feature of Siebke's recent thorough study of the hormone excretions of women during the menstrual cycle is the constant finding of the male hormone in the urine, though not in the feces. From a quantitative standpoint, the amount is not at all negligible, a liter of



Formula 1.—Showing the structural chemical similarity between the male hormone (androsteron) and the follicle hormone. Note in each the three hexagonal rings of the phenanthrene nucleus (Butenandt).

urine containing an amount of the male hormone worth in Germany 10 R.M., at the present marked value of the substance. Indeed, Siebke suggests female urine as a conveniently available source for the production of the hormone. A more striking incongruity is seen in the case of horses, for the urine of both the mare and the stallion is rich in estrin.

While the finding of the male hormone in women might theoretically be explained as due to the secretory activity of the potentially testicular elements normally present in the region of the rete ovarii in all women, and while this explanation is still favored by some, it is difficult to explain on corresponding histologic grounds the presence of the female hormone in the urine of males. It seems more likely that the reason is to be sought in the recently demonstrated closeness of chemical relation between the male and female principles. Again we see in each the same phenanthrene nucleus, and the molecular formula of the male hormone

differs from the female only by a molecule of water and an atom of carbon. Zondek has recently suggested that in both sexes the male hormone is first produced, being converted by dehydration into the female, probably under the influence of the metabolic processes which many consider to be of underlying importance in the matter of sex determination. This explanation would obviously not apply to the paradoxical conditions existing in the equine family above alluded to.

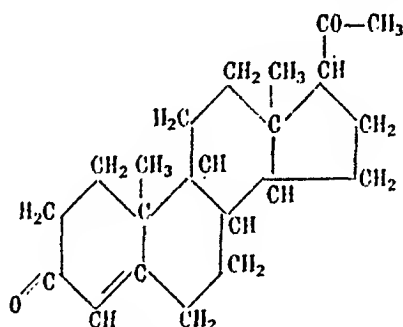
It will thus be seen that this newly discovered chemical relation of the male and female hormones is of fundamental importance as regards the questions of sex specificity, sex differentiation, and intersexuality. More and more evidence is accruing to show that the cells of either sex type of gonad are capable of producing either male or female hormones. As just one instance may be mentioned the cases of intersexuality which are characterized by dominantly female characteristics even though the only gonads present are testes. This is illustrated in a recent case of my own, more fully described in a paper recently presented before the Section on Pathology and Physiology of the American Medical Association. It is also well exemplified in the recent case of similar nature reported by Cadiz and Lipschütz, in which typical menopausal symptoms followed removal of the patient's testes. There is a considerable mass of evidence to the same effect available from the experimental laboratory.

It requires no great stretch of imagination to conceive of the possible bearing of such observations upon the production of intersexual conditions, particularly if one accepts the viewpoint championed by Witschi, and favored by many biologists, that the cortex of the gonad is a determiner of femininity and the medulla a determiner of masculinity in the germ cells. In other words, a germ cell developing in the cortex will become an oöcyte, that in the medulla a spermatocyte. This has been clearly established in such animals as the frog, and there is much to support it as regards the higher forms. If such facultativeness is exhibited by the dominating germ cells themselves, it would not be surprising if the character of the sex hormones also were susceptible of modification by environmental conditions.

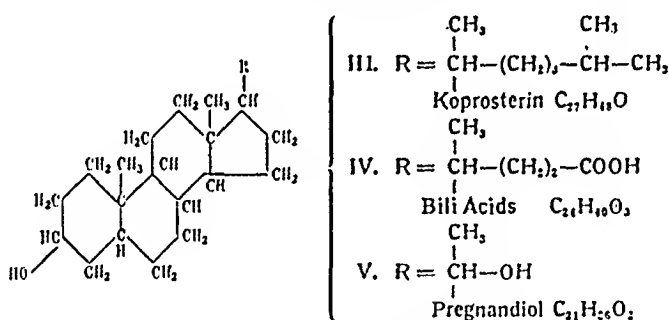
The immediate advantage of securing the sex hormones in pure form is that it will make possible more precise study of their physiologic rôles. By contrast, the inability to prepare the various anterior pituitary hormones in pure form has been the greatest handicap in the study of their physiologic action, not to speak of their therapeutic application. Again, it has already been shown that the potency of estrin preparations is susceptible of enormous increase by means of chemical treatment, and there is even a strong possibility that they may, before very long, be produced by synthesis. A hopeful start along this line has already been made by Butenandt and others.

Just what factor it is which in the mechanism of the reproductive processes determines the transformation of estrin into progesterin, if such a transformation does occur, cannot be stated, though the obvious suggestion would be that it is dependent upon the interrelationships between the ovarian and pituitary functions, just as this interrelationship apparently determines the transformation of granulosa into lutein cells. Not only in the normal mechanism but also in certain pathologic conditions is there seen such a transformation of granulosa into lutein morphology and function.

For example, in the well-known granulosa cell group of ovarian tumors, one may occasionally find a metamorphosis of granulosa cells into lutein-like cells (granulosa cell carcinoma lipidique), and this change



Formula 2.—Structural formula of the corpus luteum hormone or progesterin (Butenandt).



Formula 3.—Showing close relationship between koprosterin, the bile acids, and pregnandiol, an estrogenic substance found in the urine of pregnant women (Butenandt).

in morphology is reflected in the appearance of a decidual or predecidual picture in the endometrium. Such an endometrial response cannot, so far as we know, be brought about by any factor save progesterin, and there would seem to be no other source for the latter except the modified granulosa cells. In a case of this type recently reported by Novak and Brawner, the patient was ten years beyond the menopause, and there were, of course, no functioning corpora lutea in the ovaries.

There is still another angle of this new chemical work which has excited intense interest among investigators. I refer to the discovery of the close chemical relation which apparently exists between the sex hormones and the well-known sterol group of chemicals, and particularly the so-

called carcinogenic substances, such as certain tar derivatives. Here contact is made with the most important of medical problems, that of cancer in general, and the rush of investigators to this new line of approach is ample evidence of the possibilities which it is believed to offer.

With the sterol substances, including cholesterol, as with the bile acids, we have again to deal with the same three hexagonal rings of the phenanthrene nucleus which characterizes the three gonadal hormones. Curiously enough phenanthrene itself is inert so far as any biologic effect upon the genital tract is concerned. On the other hand, as Dodds and others have shown, certain of the sterols, when injected into castrated female animals, bring about definite estrous effects. This rather startling observation would make us question the specificity of the hormones to which alone such biologic effects have hitherto been ascribed. It would also seem to throw light on the occurrence of estrogenic principles in various bituminous minerals, and in coal, peat, petroleum, and crude oil. The presence of biologically potent chemicals seems to offer a more probable explanation for this than does the view that these substances contain the locked-up and still active female sex hormone existing in the plant life of millions of years ago. That hormones play an important part in plant life is now apparently well established.

Most provocative of all, however, is the fact that certain of the sterol substances are not only estrogenic but also carcinogenic. There are a certain number of circumstantial observations which even before this had suggested some sort of relation between the endocrine organs and cancer, such as the frequent positiveness of the Aschheim-Zondek test in cases of female genital cancer, and the finding of large amounts of estrin in the blood of cancer patients, even when these are males. To these might be added the results of many experimental studies during the past few years, such as those of Murray, Cook and Dodds, Overholser and Allen, Hofbauer, Geschickter, Lewis and Hartman, and Lacassagne. The last named, for example, has reported the production of mammary cancer in three male mice, in a strain in which this disease spontaneously affects only the female, by means of the injection of oily solutions of estrin.

To say, as some are already saying, that cancer is perhaps produced by derivation or deterioration products of the hormones, is certainly unjustified and premature, but, on the other hand, the possibility that the closed door of cancer may sooner or later be unlocked by an endocrine key has been made more real by the chemical studies we have been discussing. On the other hand, it is only fair to state that some investigators, notably Loeb, are considerably less enthusiastic about the possibilities in this field. In his recent review of the subject, this author states that "while carcinogenic hydrocarbons as well as regenerative processes (irritation) may affect a great variety of tissues, the estrogenic

hormones are limited in their action to the tissues in which they induce growth processes during the normal sexual cycle." In any event, the next few years are sure to be exciting ones to those now pushing forward along this new line of investigation.

#### THE PARTICIPATION OF THE POSTERIOR HYPOPHYSEAL LOBE AND THE MIDBRAIN IN THE CYCLE

In all discussions of the mechanism of menstruation, it is upon the endocrine factors that much the heaviest accent has been laid, first those originating from the ovary, more latterly also those arising in the anterior lobe. Indeed, almost nothing is known of any other cogs in the menstrual machinery, though some must be of great importance. It is of interest, therefore, to note that physiologists are now probing deeper than the anterior hypophysis in the elusive search for the "deus ex machina" of the reproductive cycle. We must now encompass in our discussions of the subject at least a nebulous consideration of the probable rôles of the posterior pituitary lobe, the hypothalamus, and the floor of the third ventricle, and already a sexual center, located somewhere in the midbrain, has been postulated.

Perhaps the first intimations that the parahypophyseal portions of the midbrain play a part in the reproductive cycle emanated from the long discussion as to the seat of disturbance in certain abnormalities of the cycle, and especially in the so-called hypopituitary amenorrhea associated with the adiposogenital dystrophy of Fröhlich. This is not the place to review the fluctuations of the discussion throughout many years. Suffice it to say that there now seems to be general acceptance of Smith's convincing demonstration that the metabolic disturbances of this syndrome are of hypothalamic and not of pituitary origin, though the anterior hypophysis is responsible for the sex changes.

The exact nature of the hypophyseocerebral relationship is not known, and certainly there is no widespread acceptance of the view that the mingling of effects is due to an invasion of the hypothalamus by hypophyseal cells. At any rate, we can no longer hew too closely to the hypophyseal line in the consideration of the metabolic disturbances which are so often associated with amenorrhea. There is as yet no evidence, however, to indicate that an extrahypophyseal factor may be concerned in the frequent transitory weight increase of the normal human cycle. Attention has been recently called to these by Sweeney, as a result of weight studies of 42 normally menstruating women. In 30 per cent of these, he found an increase of 3 or more pounds during the period.

My own experience convinces me of the general correctness of Sweeney's observations. I have been especially interested in the group of cases first described by Thomas in 1933, in which the menstrual weight

increase was exaggerated, and was obviously due to a generalized edema. I have seen four such cases in the past two years. In one of these the gain of weight was as much as fifteen pounds, and the edema during the menstrual period was very obvious, with swelling of the face tissues, puffiness of the eyelids, and swelling and pitting of the feet and ankles. In two of the patients in whom there was an opportunity for fairly complete study, it was easy to demonstrate marked fluid retention during menstruation, with polyuria and rapid disappearance of the edema after the period.

Of especial interest was a patient of twenty-one who suffered with complete amenorrhea of three years' duration, together with enormous adiposity, her weight being 232 pounds. She responded quite favorably, so far as weight was concerned, to a low calorie diet, together with the administration of moderate doses of thyroid, even though her basal metabolism rate was very little below normal. Her weight dropped to 185 during the period of several months she was under observation, but this drop in weight was punctuated by sharp rises of from seven to ten pounds occurring rather regularly at three-week intervals. It was not uncommon for this patient, almost over night and with no intake of fluid or food, to show this sharp rise of weight, and this was accompanied by a lowered output of fluid and visible evidence of mild edema. In other words, she exhibited a three-week metabolic cycle even though there was no cycle of menstrual bleeding. At the end of four months, and possibly as a result of light hypophyseal radiation, she began to menstruate, her periods of bleeding coinciding with the weight increase.

A search of the literature has shown the meagerness of our knowledge concerning this interesting phenomenon of menstrual edema. It presents some points of similarity and some of dissimilarity to the so-called Epstein nephrosis, which, however, is not a cyclic phenomenon. The first and almost the only laboratory studies of the subject appear to be those of Eufinger and his collaborators. In Eufinger's first paper, in 1928, he found that 30 per cent of normally menstruating women exhibit a lessened stability of the blood colloids. In another paper of the same year, with Goldner, it was shown by studies of the blood proteins that during menstruation there is a sharp rise in the level of globulin, which may be even doubled, while the albumin level drops correspondingly. Usually by the end of menstruation the globulin content has again dropped to normal, and the albumin has risen to its former level.

In a third paper, with Spiegler as collaborator (1928), based on a study of twenty-five normally menstruating women, he presents evidence to indicate that this physicochemical disturbance of colloid structure is linked up with water metabolism, leading to water retention during menstruation. Incidentally, as Eufinger and Spiegler show, there has been much difference in the results of studies upon a possible chloride



retention during menstruation. In 47 per cent of the cases studied, these authors demonstrated a water retention and tendency to edema during menstruation and at times during the immediately premenstrual period.

In these days of endocrine explanations, it is hard to avoid thinking of the posterior lobe as in some way linked up with this phenomenon of cyclical water retention, and of theorizing that this structure, so overshadowed in gynecologic interest by the anterior lobe, may participate in the cyclical changes of menstruation, and that in some way its admittedly antidiuretic function is increased during menstruation. The problem is, of course, not so simple as all this, as one will soon learn if one begins to look into the intricacies of water balance. A very superficial peep was enough to discourage me from attempting any discussion of this problem.

My reason for including the subject in this paper was simply to stress the fact that in the endocrinopathic weight increases so frequently observed in gynecologic practice, one must take cognizance not only of a metabolic disturbance characterized by actual deposit of fat, but also of the factor of water and possibly chloride retention, manifested in some degree even in many normally menstruating women and to a more striking degree in the occasional cases of generalized menstrual edema. It is quite certain that these two types of disturbance may coexist in the same patient.

From what has been said, it will be seen that there is considerable justification for the view that the cycle of menstruation involves not only the endocrine glands, but that certain areas of the brain are involved also. Still other evidence along this line is available in the recent studies of Hohlweg and Junkman upon the reverse effect of the follicle hormone upon the anterior lobe. The work of Kunde, d'Amour, Carlson and Gustavson, that of Meyer, Leonard, Hisaw and Martin, Moore and a host of other investigators, have established the fact that continued injection of sufficiently large doses of estrin brings about inhibition of the anterior pituitary sex hormone function. This general conclusion is not invalidated by the recent paper of Clauberg and Breipohl, in which it appeared that a single large injection of estrin was followed by a sharp increase in anterior pituitary activity. The latter conclusion, moreover, still needs confirmation.

The special interest of the contribution of Hohlweg and Junkman lies in their conclusion that the inhibition of the anterior lobe is not a direct one upon the gland, but that it is mediated through a sex center in the midbrain. If, for example, a second hypophysis is implanted into the kidney and the animal later castrated, only the normal hypophysis and not the implanted one shows the well-known castration changes. The conclusion therefore is reached that the effect on the normal pituitary is not a direct blood borne one, but that it must be exerted through

nervous channels, affecting the normal gland but not the implanted one. Hohlweg and Junkman therefore conclude that there must be a "sex center," located in all probability in the floor of the third ventricle, as indeed had been previously suggested by Teel and Cushing as a result of the study of the effects of tumors in this region. Schoeller suggests that this concept would explain the fact, first demonstrated by Philipp, that the hypophysis of the pregnant woman contains so little of the gonadotropic principles in spite of their abundance in the urine.

In all these studies there is manifest a strong new trend to seek beyond the endocrine glands for an explanation of the phenomena of the

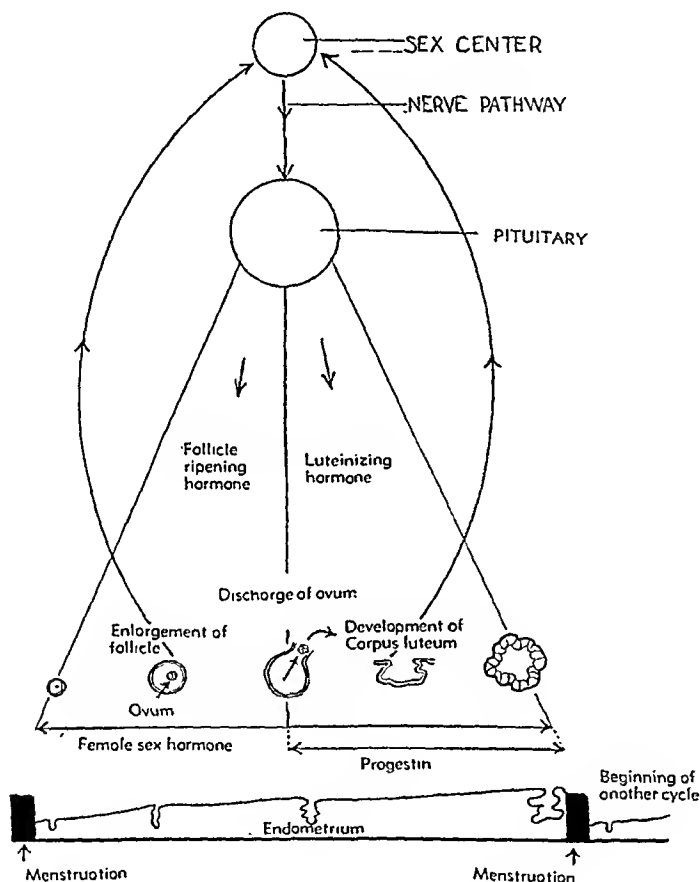


Fig. 1.—Showing the probable mechanism by which the reverse inhibitory effect of the gonads upon the anterior hypophysis is produced, i.e., through the agency of a "sex center" in the midbrain and nerve pathways to the anterior lobe. (Adapted from Hohlweg and Junkman.)

menstrual cycle, as if there were not enough factors already to bedevil and confuse those trying to keep up with the march of developments. As shown in Fig. 1, we must now add another link to the diagrams which have become so popular in the representation of how menstruation is brought about.

The chief significance of this extension of viewpoint would seem to be that it, for the first time, links up the endocrines and the nervous system. That they are closely coordinated has always seemed certain

on mere a priori grounds, for both are parts of the body's system of intercommunication, one primitive, the other highly developed. Even psychic factors have been generally accepted as possible causes of menstrual disturbances, and a beginning has apparently been made in exploring the pathways involved. Again, we may quite possibly have advanced a few steps toward an explanation of the vasomotor phenomena of the menopause, associated as they are with certain hormonal body changes, and yet so clearly involving nerve pathways. And the examples might be multiplied.

#### THE ANOVULATORY TYPE OF CYCLE

The possible occurrence of a periodic uterine bleeding which clinically is indistinguishable from menstruation, but which is not associated with ovulation, is now established beyond all doubt. The early work of Corner, abundantly confirmed by Hartman and Allen, had shown that the anovulatory type of cycle is very common in monkeys, which resemble the human being quite closely so far as the reproductive mechanism is concerned. Van Herwerden had, indeed, maintained this possibility as far back as 1906. Some years ago Corner urged that this anovulatory type of cycle is found also in some women, though unquestionably in the vast majority ovulation and corpus luteum formation play essential rôles in the menstrual cycle. When, in 1934, as in several previous papers, I likewise emphasized the possibility of human menstruation without ovulation, and urged this as the explanation of some cases of sterility, a miniature international discussion was precipitated by Shaw, of London, who very generously diffused his criticism of my own views so as to include the distinguished laboratory investigators whom I have named above.

Since then a continuation of my own studies, as well as investigations in other large clinics, has conclusively shown the not infrequent occurrence of the anovulatory type of menstrual cycle. Tietze, from Schröder's clinic at Kiel, reports finding it in 31 of 466 cases of periodic bleeding. Mazer and Ziserman report the finding of a non-ovulatory endometrium in twenty-four of forty-one regularly menstruating but functionally sterile women, a proportion much greater than I have encountered in my own work. Other authors reporting a considerable incidence of anovulatory cases are Fluhmann and Morse, Adler, and Anspaeh and Hoffman.

What is the mechanism of the menstrual cycle in these cases in which ovulation is lacking? Just after a menstrual bleeding, a group, probably a considerable group, of follicles begins to mature and soon to produce increasing amounts of estrin, just as in the usual ovulatory mechanism. Unlike the latter, however, rupture of a single follicle which has outstripped its fellows fails to occur. In some cases, it is true, there is a single dominating follicle, often becoming large and cystic, as one

not infrequently finds in cases of functional bleeding associated with hyperplasia of the endometrium. In other cases, and I believe even more frequently, one finds a considerable group of follicles developing to various stages without actually reaching full maturity, though all of them produce estrin. In the latter group one finds the small multiple cysts which are so often seen in the ovaries of the functional bleeding group. The important defect is in the ovulating principle, whatever this may be. The evidence points more and more to the probability that ovulation is produced, not by any one pituitary or ovarian principle, but that it occurs at a "drehpunkt" which is produced by a delicate quantitative balance between various hormonal factors.

In the typical functional bleeding case, the follicle is likely to develop, without rupturing, beyond the stage of usual maturity, after which a dehiscence sets in, with death of the ovum, degeneration of the granulosa, and cessation or marked diminution of estrin production. This is followed, after a variable number of days, by bleeding, most frequently an interval longer than normal because of the lengthened life span of the follicle. But this is not invariably so, for the retrogression of the follicle may begin sufficiently early to make the intervals between bleedings quite like those of menstruation, while the amount and duration of the bleeding likewise may resemble that of normal menstruation.

Thus is produced a periodic bleeding which, as I have said, is indistinguishable from normal menstruation, though at times there is some irregularity and some excess above the usual menstrual amount. Bleeding of this type is, in my experience, most often encountered in women approaching middle life, as well as in young adolescent women, though it may be seen at any age during reproductive life. The age distribution, in other words, is quite like that of functional bleeding, of which it may be considered a mild form. Whether or not it is always to be considered pathologic, even when menstruation is ostensibly proceeding normally, is a matter of definition. There is no possible way of distinguishing this type of cycle clinically from the usual ovulatory type except by microscopic examination of the endometrium, and this should be done when there is some clear clinical need for such information, as in cases of sterility in which all other factors have been ruled out.

The endometrium will yield the necessary information only if studied shortly before an expected flow. In the usual ovulatory cycle there is then present in the ovary a large, functioning corpus luteum, producing progesterin, and bringing about the characteristic secretory phenomena in the endometrium. If, however, the endometrium shows only one type or another of proliferative endometrium, with no evidence of secretion, one may conclude that there is an absence of progesterin, that no functioning corpus luteum is present in the ovary, and that therefore ovulation has not occurred. Usually the distinction between the secretory and non-

secretory types of endometrium is possible from histologic examination alone, although it can, and usually should, be confirmed by differential staining for glycogen.

A typical case of this group is represented by the patient whose endometrium is shown in Fig. 2. She is twenty-eight years old, and both she and her husband have been repeatedly examined and found normal by competent clinicians in New York and Baltimore. The couple had been married seven years, with no pregnancies. Menstruation, the dates of which had been carefully recorded for many years, recurred at quite regular thirty-day intervals, the flow lasting five days, and being moderately free. By way of parenthesis, I may add that, like many others, I am very skeptical of the accuracy of menstrual dates unless properly recorded by the patient. An aspiration curettage done on the



Fig. 2.

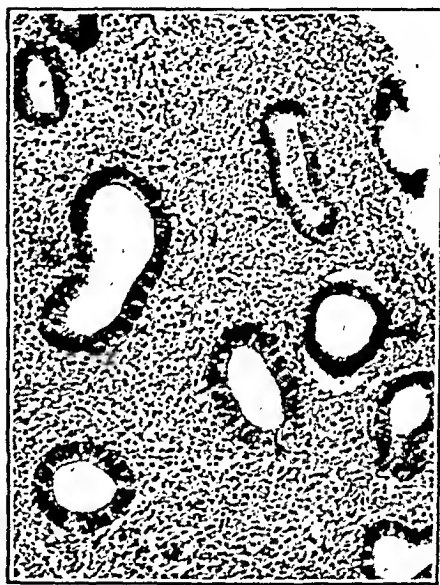


Fig. 3.

Fig. 2.—Proliferative, nonsecretory endometrium obtained by suction-curette from uterus of a sterile woman of twenty-eight years on twenty-ninth day of thirty-day cycle. (See text.)

Fig. 3.—Nonsecretory endometrium, resembling early interval type, removed on twenty-fourth day of twenty-eight-day cycle.

twenty-ninth day of the cycle showed the endometrium depicted in Fig. 2. It is of a nonsecretory hyperplasia pattern, so that ovulation had obviously not occurred. Another instance of the same type is shown in Fig. 3.

As to the incidence of the anovulatory cases in our own material, I cannot as yet give any accurate figures, though the question is now being studied in our laboratory by Dr. Howard C. Jones. I can only repeat the statement I have made in previous papers, that the anovulatory mechanism is certainly the exceptional one among women in general, but that it is not rare in the small group of sterility cases in which all other factors can apparently be excluded. The microscopie examination of

the premenstrual endometrium in the anovulatory cases will show either a proliferative picture similar to that seen in the interval phase of the usual menstrual cycle, or it will show a greater or lesser degree of hyperplasia, with at times a definite Swiss-cheese pattern.

The technic which we employ in securing tissue for study was recently described in the *Journal of the American Medical Association*, so that it need not be discussed here. Suffice it to say that the aspiration curette-cannula which we have devised, for use with the electric motor suction apparatus, has been highly satisfactory for this purpose, and for many others. It takes only a few moments, almost never requires an anesthetic, causes no great pain, and makes hospitalization unnecessary.

We have extended the use of this technic to various other indications. For example, when adenocarcinoma of the fundus is suspected, aspiration curettage is done without anesthesia, the microscopic examination made at once, and, if malignancy is found, the radical operation proceeded with. In a recent patient, again, one of my colleagues demonstrated tuberculosis of the endometrium, although this had not been suspected. I would again call attention to the rich possibilities of this simple technic in studying the condition of the endometrium in cases of endocrinopathic amenorrhea, for undoubtedly a cycle occurs in some patients even though there is no bleeding phase. Finally, a systematic study by this method, in patients in whom coitus is properly timed in relation to the menstrual periods, is quite sure sooner or later to make embryologists happy by the finding of fertilized eggs at stages much earlier than the Miller ovum, possibly of eggs not yet implanted.

#### ENDOCRINE FACTORS IN MENSTRUAL BLEEDING

Only very brief attention need be called to certain new aspects of a problem which is anything but new. I refer to the question of the hormone mechanism of menstrual bleeding. As this has been more fully discussed elsewhere, I shall state simply that the evidence of recent years has seemed to indicate that the responsible factor is a withdrawal or sharp drop in the estrin blood level, thus "knocking the props," as it were, from the endometrium which had been built up under hormonal stimulation. It was rather generally accepted that the catabolic phase thus induced in the endometrium is responsible for its desquamation, with the accompanying bleeding which we call menstruation.

There has always, however, been a minority of investigators who believe that the responsible factor is the withdrawal of the corpus luteum secretion, progesterin. The recent work on the chemical kinship of estrin and progesterin makes this difference of viewpoint seem less sharp and less important than formerly, but it is of interest to note that two very authoritative investigators, Engle and Smith, have very recently pro-

duced evidence to support the minority view that withdrawal of progestin rather than of estrin is the endocrine factor of prime importance in precipitating the actual bleeding of menstruation. Through the courtesy of Dr. Engle, I have had the opportunity of reading this paper in advance of its publication in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*, and of making use of the conclusions which were reached.

It would appear, however, that the broad concept of menstrual bleeding as a phenomenon due to endocrine withdrawal remains unchanged. Furthermore, the view that the ovarian hormone drop is induced by a reciprocal inhibiting effect upon anterior pituitary function still seems the most tenable, especially as Clauberg and Breipohl have recently shown that the inhibitory changes produced in the pituitary by progestin and demonstrable by histologic study are quite similar to those produced by estrin. Nor is there any new evidence to change our viewpoint as to the mechanism of the purely estrin-induced type of bleeding, exhibited clinically in so-called functional bleeding and in the occasional case of anovulatory menstruation, or, if one prefers the term, "pseudomenstruation."

#### SUMMARY

This paper deals with several problems in the field of reproductive physiology, chosen because of their newness and their importance, and because they indicate new trends in this field. The most outstanding advance of the past few years is the recent work on the chemistry of the male and female gonadal hormones (estrin, progestin, androkinin), indicating as it does the close chemical kinship of all three. Furthermore, a similarly close relation has been demonstrated between these hormones and certain well-known chemical substances of the sterol group, as well as the bile acids, certain vitamins, and certain carcinogenic substances. This last named relationship has sent investigators off full cry on a new scent, and it is even possible that the cancer problem may be unlocked with an endocrine key.

While hitherto reproductive physiology has been concerned almost entirely with endocrinology, investigators are beginning to go beyond the endocrine glands in explaining certain cyclical phenomena, and to speak of a sex center located somewhere in the midbrain. Certain cyclical disturbances of menstruation would seem to justify such an assumption and to suggest also a possible participation of the posterior lobe. One of the most interesting phenomena coming under this head is the weight increase and edema seen in many women at menstruation, and in exaggerated form in the so-called generalized edema of menstruation. This type of cyclical water balance disturbance may be seen even in the absence of a bleeding cycle. Its exact mechanism is not known, but its occurrence seems in some way linked up with a change in the globulin-albumin proportions of the blood serum.

Reference is made again to the undoubted possibility that periodic bleeding, clinically interpreted by the patient as normal menstruation, may occur without ovulation. The bearing of this on the study of sterility is obvious, for it undoubtedly explains some cases. The technic which we have found most satisfactory in determining whether or not a patient is ovulating is briefly described.

Finally, brief reference is made to recent investigations suggesting that menstrual bleeding is due to withdrawal of progestin rather than of estrin, as has been generally accepted. Because of the now well-established chemical relation between estrin and progestin, and the fact that they exert a similar inhibiting effect upon the hypophysis, there is no material change in the general concept of the mechanism responsible for the bleeding of menstruation.

## REFERENCES

- Aschheim, S.*: Arch. f. Gynäk. 132: 179, 1927. *Butenandt, A.*: Deutsche med. Wchnschr. 55: 2171, 1929; Ztschr. f. physiol. Chem. 208: 129, 1931; Ibid. 210: 268, 1932; Zentralbl. f. Gynäk. 59: 71, 1935. *Doisy, E. A., Veler, E. D., and Thayer, S. A.*: J. Biol. Chem. 86: 499, 1930. *Marrian, G. F.*: Biochem. J. 24: 1021, 1931; Physiol. Rev. 13: 185, 1933. *Siebbe*: Arch. f. Gynäk. 156: 317, 1934. *Schoeller, W.*: Deutsche med. Wchnschr. 58: 1531, 1932; also Lancet 1: 38, 1933. *Allen, W. M.*: Am. J. Physiol. 92: 174, 1930. *Fels, K., Slotta, K. H., and Ruschig, H.*: Klin. Wchnschr. 13: 1207, 1934. *Butenandt, A., Westphal, U., and Hohlweg, W.*: Ztschr. f. physiol. Chem. 227: 84, 1934. *Zondek, B.*: Lancet 2: 356, 1934. *Cadiz, R., and Lipschütz, A.*: Arch. f. Gynäk. 153: 593, 1933. *Witschi, E.*: Sex and the Internal Secretions. Edited by Edgar Allen. Baltimore, 1932, Williams & Wilkins Co., Chapter V. *Novak, E., and Brawner, J. H.*: AM. J. OBST. & GYNEC. 28: 637, 1934. *Dodds, E. C.*: Lancet 1: 931, 1934. *Murray, W. S.*: J. Cancer Res. 12: 18, 1928. *Cook, J. W., and Dodds, E. C.*: Nature 131: 205, 1933. *Overholser, M. D., and Allen, E.*: Surg. Gynec. Obst. 60: 129, 1935. *Hofbauer, J.*: Zentralbl. f. Gynäk. 54: 2393, 1930. *Geschickter, C., Lewis, D., and Hartman, C. G.*: Am. J. Cancer 21: 828, 1934. *Lacassagne, A.*: Compt. rend. Acad. d. sc. 195: 630, 1932. *Loeb, L.*: J. A. M. A. 104: 1597, 1935. *Smith, P. E.*: J. A. M. A. 88: 158, 1927. *Smith, P. E., and MacDowell, E. C.*: Anat. Rec. 46: 249, 1930. *Sweeney, J. S.*: J. A. M. A. 103: 234, 1934. *Thomas, W. A.*: J. A. M. A. 101: 1126, 1933. *Eufinger*: Monatschr. f. Geburtsh. u. Gynäk. 74: 139, 1926. *Eufinger, H., and Goldner, M.*: Monatschr. f. Geburtsh. u. Gynäk. 73: 62, 1926. *Eufinger, H., and Spiegler, R.*: Arch. f. Gynäk. 135: 223, 1928. *Hohlweg and Junkman*: Arch. f. d. ges. Physiol. 232: 148, 1933. *Kunde, M., d'Amour, C., Carlson, A. J., and Gustavson, R. G.*: Am. J. Physiol. 95: 630, 1930. *Meyer, R. K., Leonard, S. L., Hisaw, F. L., and Martin, S. J.*: Proc. Soc. Exper. Biol. & Med. 27: 702, 1930. *Moore, C. R.*: Proc. 2nd Int. Congress Sex Research, p. 293, 1930. *Clauberg, C., and Breipohl, W.*: Klin. Wchnschr. 14: 119, 1935. *Teel, H. M., and Cushing, H.*: Endokrinologie 6: 401, 1930. *Philipp, E.*: Zentralbl. f. Gynäk. 54: 450, 1930. *Corner, G. W.*: J. A. M. A. 89: 1838, 1927. *Hartman, C. G.*: Anat. Rec. 35: 13, 1927. *Allen, E.*: Contrib. Embryol. (No. 98). Carnegie Inst., Washington 19: 1, 1927. *van Herwerden, M.*: Monatschr. f. Geburtsh. u. Gynäk. 24: 730, 1906. *Novak, E.*: Brit. M. J. 2: 553, 1933; also Practitioner 132: 313, 1934. *Tietze, K.*: Arch. f. Gynäk. 156: 35, 1934. *Mæzer, C., and Ziserman, A. J.*: Am. J. Surg. 18: 332, 1932. *Fulmann, C. F., and Morse, D. L.*: AM. J. OBST. & GYNEC. 21: 455, 1931. *Adler, K.*: Monatschr. f. Geburtsh. u. Gynäk. 90: 340, 1932. *Anspach, B. M., and Hoffman, J.*: AM. J. OBST. & GYNEC. 28: 473, 1934. *Novak, E.*: J. A. M. A. 104: 1497, 1935. *Hartman, C. G., and Novak, E.*: Curtis' Obstetrics & Gynecology, Philadelphia, 1933, W. B. Saunders Co., Chapter IX. *Engle, E. T., and Smith, P. E.*: AM. J. OBST. & GYNEC. 29: 787, 1935. *Clauberg, C., and Breipohl, W.*: Klin. Wchnschr. 14: 119, 1935. *Engle, E. T., and Smith, P. E.*: AM. J. OBST. & GYNEC. 29: 787, 1935.



## EXPERIENCES WITH AMNIOTIN IN THE TREATMENT OF GONOCOCCAL VAGINITIS IN CHILDREN\*

RICHARD W. TELINDE, M.D., AND JAMES N. BRAWNER, JR., M.D.,  
BALTIMORE, Md.

*(From the Department of Gynecology, Johns Hopkins University)*

THAT the treatment of gonocoeccal vaginitis with the various chemical disinfectants has, thus far at least, proved to be most unsatisfactory is generally recognized. In our clinic in a series of 50 cases, the average duration of treatment before consistently negative smears were obtained was four months, and the average period of treatment and observation before it was thought safe to discharge the patients was six months. The report of the Bellevue-Yorkville Project,<sup>1</sup> published in 1933, affords ample proof that little progress has been made along the lines of treatment by chemical and vaccination methods. In a series of 212 cases treated with chemicals, vaccines, or a combination of both in the out-patient department, the average duration of "treatment and observation" was fourteen months. Twenty-nine patients were hospitalized and were under "treatment and observation" for an average of 5.3 months. That vaccine is of no value was demonstrated by the fact that a control group which received no treatment improved more promptly than the group receiving vaccine alone. More recently attempts have been made to cure the disease by the use of diathermy. In 1933, R. J. Crossen<sup>2</sup> reported fifteen patients treated by this method. Ten of his cases were classified as acute and required treatment for 21.6 weeks before a consistently negative smear was obtained. In five chronic cases 4.6 weeks were required. Moreover, the practical difficulties in applying this method of treatment to young children are considerable.

In the adult vagina the mucosa is composed of stratified squamous epithelium twenty-five to forty layers deep (Fig. 1, *B*). It is a well-known clinical fact that the adult vagina is resistant to gonocoeccal infection. In the prepubescent vagina the vaginal mucosa is thin and delicate, composed, as it is, of immature squamous epithelial cells six to fourteen layers deep (Fig. 1, *A*). Its susceptibility to infection by the gonococcus is well known. At puberty the vaginal epithelium undergoes a change to the adult type, and a gonocoeccal vaginitis existing at this time is observed to subside. Following the work of Allen,<sup>3</sup> who showed that the thin vaginal epithelium of immature animals could be

\*Supported by a research grant from E. R. Squibb and Sons.

transferred into the adult type by the injection of estrin, it occurred to Lewis<sup>4</sup> that if this change could be produced in the vaginal epithelium of children suffering from vaginitis, a cure was possible. He reported eight cases of gonococcal vaginitis in children treated two or three times daily with 50 units of estrin hypodermically over an average period of twenty-one days. In all these cases the infection cleared. Biopsies from the vagina revealed a definite change in the epithelium from the infantile to the adult type. The infection recurred in two of his cases, one of which was treated again successfully.

We felt that the results of Lewis' small series were sufficiently encouraging to warrant a more complete investigation of the value of the estrogenic hormone in treating this disease. Since March, 1934, we have treated a total of thirty-five patients with the estrogenic preparation,

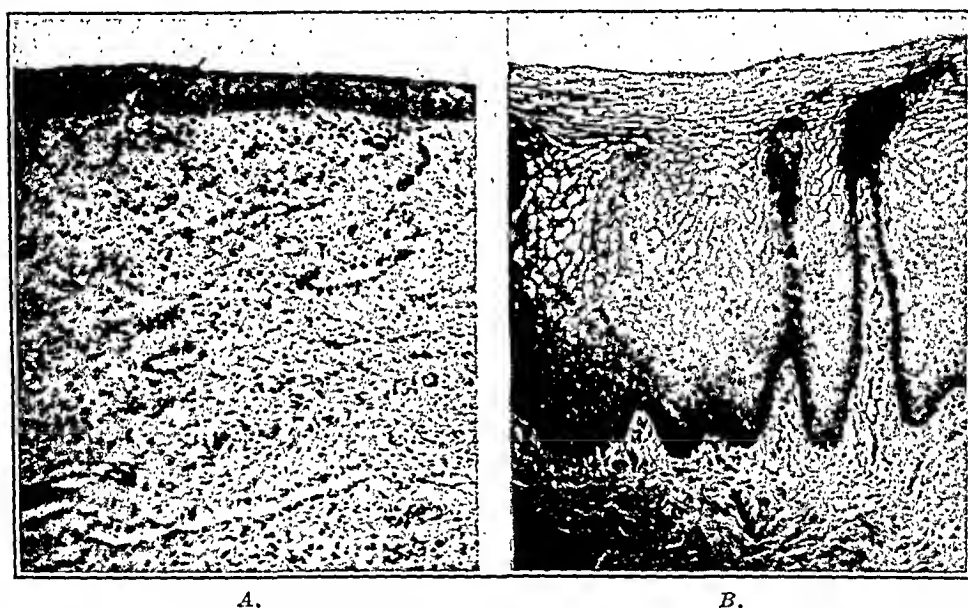


Fig. 1.—A, Normal vagina of a patient fourteen months of age, autopsy. B, Normal adult vagina of a patient thirty-seven years of age.

*amniotin*, administered orally, hypodermically, and in vaginal suppositories. We sought to determine:

1. Will the administration of amniotin cure gonococcal vaginitis?
2. If so, by what method of administration and in what dosage is it most effective?
3. What changes may be noted in the genital tract and in the breasts?
4. If changes are noted in these organs, how soon do they appear and when do they disappear after withdrawal of the hormone?
5. Whether or not the administration of the hormone is harmful to the patient.

The cases selected for this study presented clinically typical vulvo-vaginitis with gram-negative intracellular diplococci in vaginal smears.

Twenty-three of the patients had received no previous treatment. Twelve patients had been treated with vaginal instillations and irrigations without success for periods varying from two weeks to sixteen months. All local treatments were stopped for at least a week before amniotin was begun. The ages ranged from two to eleven years.

A full-time graduate nurse was employed to give the treatments and to aid us in making daily observations. The patients were brought to the dispensary at first three times a week, and later at suitable intervals. Before treatment was begun and upon each subsequent return visit, observations were made on the general health, the breasts, the abdomen, the external genitalia, the presence or absence of vaginal bleeding, and the stained smear. The character of the vaginal washings in normal salt solution was examined microscopically. The internal genitalia were palpated rectally before and after treatment. Clippings were made for microscopic study before treatment and at desired intervals thereafter.

The amniotin was administered orally to six children in daily doses ranging from 400 to 2,000 rat units. The results are given in Table I.

TABLE I. ORAL ADMINISTRATION

CASE	NO. DAYS TREATED	TOTAL UNITS AMNIOTIN	EPITHELIAL RESPONSE	VAGINAL SMEAR	RESULT
7	81	109,600	None	Positive	Not cured
11	123	191,600	None	Neg. in 116 days	Well
17	122	168,800	None	Positive	Not cured
18	118	185,200	None	Positive	Not cured
19	111	180,000	None	Positive	Not cured
26	79	158,000	None	Positive	Not cured
Average	105.7	165,533	None	All pos. except 1	Not cured 5 Well 1

TABLE II. TEN CASES TREATED WITH HYPODERMIC INJECTIONS OF ETHYLENE GLYCOL AMNIOTIN SOLUTION

CASE	NO. DAYS TREATED	TOTAL UNITS AMNIOTIN	EPITHELIAL RESPONSE	VAGINAL SMEAR	RECURRENCE	RESULT
1	70	5,400	None	Positive	----	Not cured
2-a	31	1,550	None	Neg. after 9 days	After 28 days	Not cured
2-b	7	700	None	Positive	----	Not cured
3	19	950	None	Neg. after 5 days	None	Well 1 yr.
4	47	3,650	None	Positive	----	Not cured
5	18	900	None	Positive	----	Not cured
6	15	750	None	Positive	----	Not cured
7	11	550	None	Positive	----	Not cured
8	12	600	None	Positive	----	Not cured
9	5	500	None	Positive	----	Not cured
10	4	400	None	Positive	----	Not cured

We found no evidence of activity of amniotin administered orally, as judged by the absence of epithelial change in the vagina. The vaginal

washings showed no desquamation of epithelium and the vaginal biopsies from all these cases showed no change. Fig. 2 shows biopsies from one of these cases (A) before treatment and (B) after the oral administration of 185,000 rat units. It is true that in one case the patient became clinically well and the spreads were negative for gonococci after one hundred and sixteen days of treatment. Nevertheless, in view of the absence of epithelial change found invariably associated with clearing up of the infection after the use of the preparations administered hypodermically and in suppositories, we are inclined to regard this single case as one of spontaneous cure, and conclude that the oral administration in such doses as we have used has no therapeutic value.

A series of ten patients were treated with daily hypodermic injections of amniotin in ethylene glycol solution. Having no preconceived idea

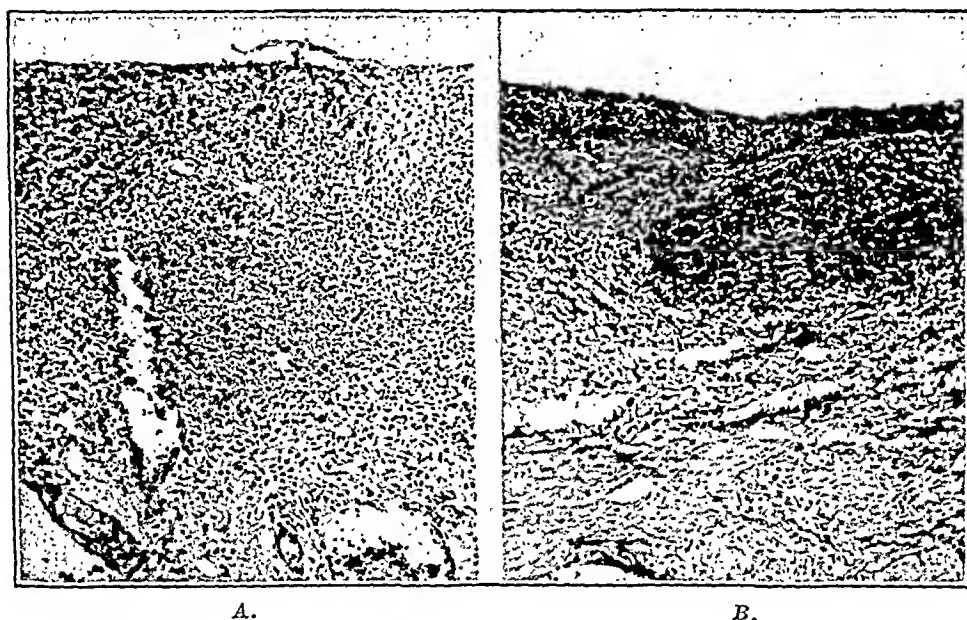


Fig. 2.—A, Case 18. Photomicrograph of a section of the vagina of a patient aged eight years. Before treatment. B, Case 18, After receiving 185,000 units over a period of one hundred eighteen days.

as to the proper dosage, we started giving 50 rat units daily. When no effect was noted, the dosage was later increased to 100 units per day. The results are given in Table II.

A glance at the chart will show that there was almost universal failure of cure with the amniotin in ethylene glycol solution. Not a single case showed any epithelial change attributable to the injections. Fig. 3 shows the epithelium (A) before, and (B) still immature, after receiving 3,650 units over a period of forty-seven days. In one of the cases the vaginitis cleared up permanently and in another it cleared up but recurred in four weeks. In neither of these cases, however, was there any evidence of hormonal action as judged by the vaginal washings or biopsy,

and we do not feel it would be fair to attribute the disappearance of the gonococcus to the hormone. Many of these patients failed to receive an amount of the hormone sufficient to afford a fair trial. The reason for this is the fact that inasmuch as no epithelial response was seen in the early cases, one of which received 5,400 units over a period of seventy days, the preparation in oil was tried. It became apparent almost immediately that the oil preparation showed evidence of much greater activity than the amniotin in ethylene glycol, and the latter, therefore, was discontinued in favor of amniotin in oil.

Having failed in our attempts to produce vaginal epithelial growth with the amniotin in ethylene glycol, we treated a series of patients

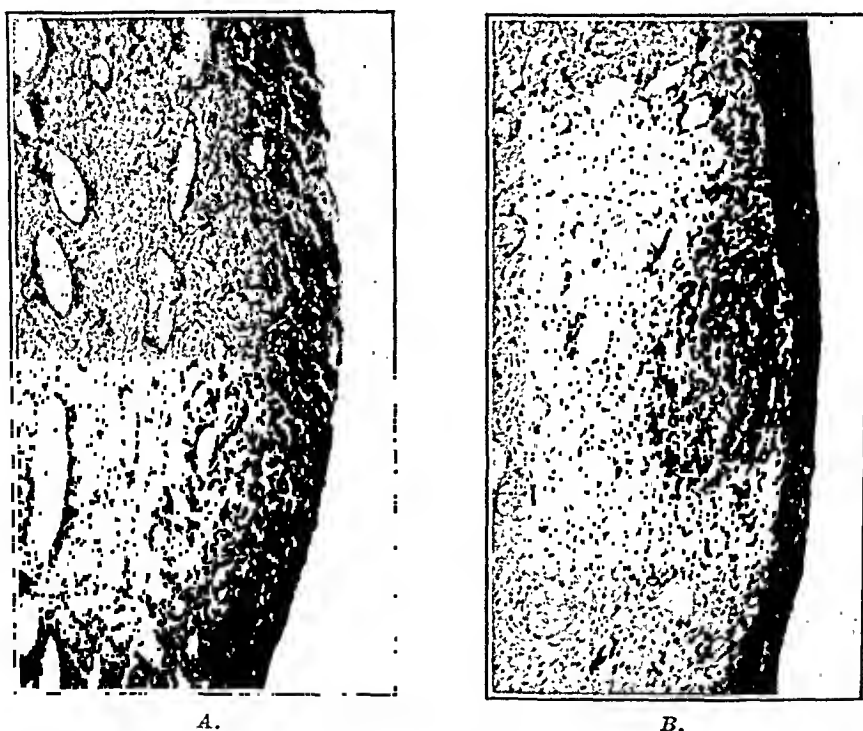


Fig. 3.—Case 4. Photomicrograph of a section of the vagina of a patient aged six years. Before treatment. *B*, Case 4. After E. G. solution hypodermically for forty-seven days, 3,560 units.

using the hormone in oil. Daily injections were given, hypodermically, in doses ranging from 50 units to 1,000 units in 1 c.c. volume. Whereas the ethylene glycol solution could be given with little discomfort to the patients, many of them complained of pain and persistent soreness following the injection of the oil solution. Obviously the oil was absorbed very slowly. This has caused us to wonder whether this slower absorption of this preparation, by maintaining a more constant level of amniotin in the tissues, might not be responsible for the better therapeutic effect. Table III summarizes our results with thirteen patients who were permanently cured with the oil preparation.

With this preparation an average of 13.5 days was required before the epithelial shedding began. Usually within a few days after the epithelial reaction became manifest in the vaginal washings, the smears became permanently negative, the average being four days after the beginning of epithelial shedding. As the epithelial desquamation begins, the pus in the vaginal washings is gradually replaced by epithelium and usually within a few days the pus has entirely disappeared and the washings consist of pure epithelium. Fig. 4 shows a typical vaginal smear before treatment, and Fig. 5 a smear from the same vagina after the drug had become effective. A biopsy taken at the latter time shows a marked thickening of the epithelium and a complete or almost complete absence of inflammatory cell infiltration (Fig. 6, B). Clinically, at this time the reddening of the vulva has largely disappeared, and the discharge may be gradually drying up although in some cases it is as profuse

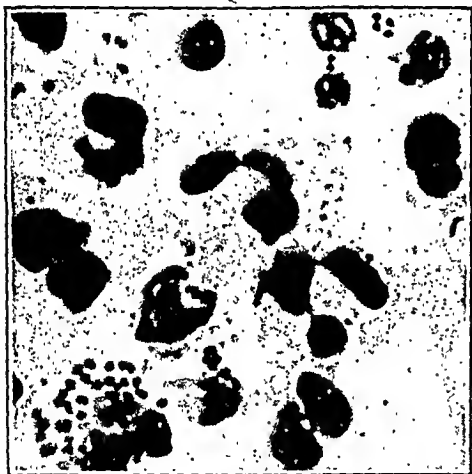


Fig. 4.



Fig. 5.

Fig. 4.—Case 24. Stained vaginal smear before treatment.

Fig. 5.—Case 24. Stained vaginal smear after fifteen days' hypodermic treatment.

as ever. In character, however, this discharge shows a decided change; instead of being purulent it has become thick and curdlike, consisting of desquamated epithelium. After the cessation of treatment this gradually disappears.

As to the optimal daily dosage, we found that the patients given 100 units per day responded as quickly as those given a larger dose. There were five patients treated with the oil preparation hypodermically in which the infection cleared up but recurred as indicated in Table IV.

The recurrences occurred on an average of 22.2 days after the cessation of treatment. Having the benefit of no previous experience, we could determine only by trial and error just how soon the treatment could be stopped after the negative smears were obtained. In the above group we stopped treatment, on an average, five days after the first permanently negative smear. This was obviously too soon and probably accounts for

the recurrences, for in the group of patients who were cured and remained well, treatment was continued twelve days after the first permanently negative smear.

TABLE III. THIRTEEN CASES PERMANENTLY CURED WITH AMNIOTIN IN OIL

CASE	AGE	NO. DAYS TREATED	TOTAL UNITS AMNIOTIN	DAYS FOR EPITHELIAL RESPONSE	DAYS FOR NEG. SMEAR	DURATION OF CURE TO DATE
1	3	24	5900	15	19	11 months
2	5	16	1600	8	12	2½ months
4	6	17	1700	7	7	11 months
8	4	32	2900	19	26	11 months
9	7	34	3400	9	28	10 months
10	6	30	3000	11	22	10 months
12	4	17	1700	7	8	9 months
13	2	16	1600	7	12	9 months
14	6	23	7500	13	19	9½ months
16	7	14	1400	8	8	9 months
17	4	34	2900	34	12	4 months
20	7	33	8250	11	25	7½ months
22	6	37	5950	26	28	7 months
Average	5.1	25.1	3600	13.5	17.5	

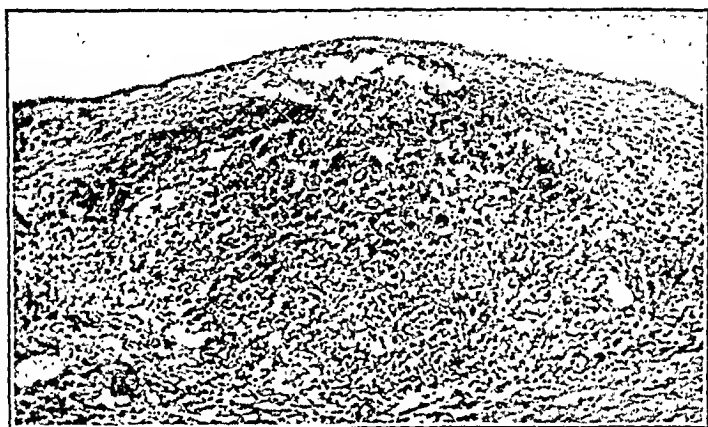
TABLE IV. RECURRENCE AFTER AMNIOTIN IN OIL (5 CASES)

CASE	AGE	NO. DAYS 1ST TREATMENT	UNITS OF AMNIOTIN	RECURRED AFTER DAYS	NO. DAYS 2ND TREATMENT	UNITS OF AMNIOTIN	DAYS FOR EPITHELIAL RESPONSE	DAYS FOR NEGATIVE SMEAR
5	3	34	2750	16	14	1400	8	10
6	9	6	300	51	71	16900	38	68
15	7	31	3100	18	22	2200	6	66
23	6	36	3600	7	52	5200	None	Pos.
25	7	66	25500	21	Suppository treatment			
Average	6.4	34.6	7050	22.2				

TABLE V. TWELVE CASES PERMANENTLY CURED WITH SUPPOSITORIES

CASE	AGE	NO. DAYS TREATED	UNITS OF AMNIOTIN IN SUPPOS.	DAYS FOR EPITHELIAL RESPONSE	DAYS FOR NEGATIVE SMEAR	DURATION OF CURE TO DATE
7	10	22	1,650	10	10	4.5 months
18	8	18	1,350	7	7	4.5 months
19	9	28	2,000	14	21	4.0 months
23	6	14	1,050	8	8	4.0 months
24	9	15	1,125	7	14	4.5 months
26	5	22	1,650	10	14	4.0 months
27	10	30	2,250	12	23	5.0 months
28	11	23	1,725	15	21	4.5 months
31	8	38	2,850	25	32	2.0 months
32	7	25	1,875	8	15	1.5 months
33	7	22	1,650	7	7	2.0 months
35	4	59	4,425	34	41	1.0 months
Average	7.8	26.3	1,967	13.1	17.8	

Among the children treated with the oil preparation there were four who were not cured; these failed to respond to the hormonal action as judged by the vaginal washings and biopsies; yet in some of the cases which failed to respond, an enormous amount of the hormone was used. In one case, 16,800 rat units were injected over sixty-three days, a much more intensive and longer treatment than was required to cure most of the cases with this preparation. The explanation for these refractory



A.



B.

C.

Fig. 6.—A, Case 16, before treatment. B, Case 16, after ten days, 100 units of oil hypodermically per day, 1,000 units. C, Case 16. Four months after cessation of treatment.

cases is not apparent, but it is worthy of note that for the most part the failures occurred in the older children of the group. The average age in the recurrent group was 8.5 years, in contrast to the average age of 5.1 years in the group who were permanently cured with this preparation.

Finally, we tried another method of adapting the estrogenic hormone to the treatment of gonococcal vaginitis. Gelatin suppositories contain-



ing 75 rat units of amniotin were used daily in a series of seventeen cases. Of these, nine had failed to respond to the oral and hypodermic methods, and eight had received no previous treatment. Inasmuch as there is a tendency to loss of a considerable portion of the suppository after melting when the patient is up and about, we recommend that the suppository be used at bedtime. The ease of administration by suppository is obvious. The results are tabulated in Table V.

From Table V it may be seen that an average of 13.1 days was required before the epithelial shedding began, and 17.8 days were required for a consistently negative smear. The average duration of treatment was 26.3 days. It is interesting to note the remarkable similarity of

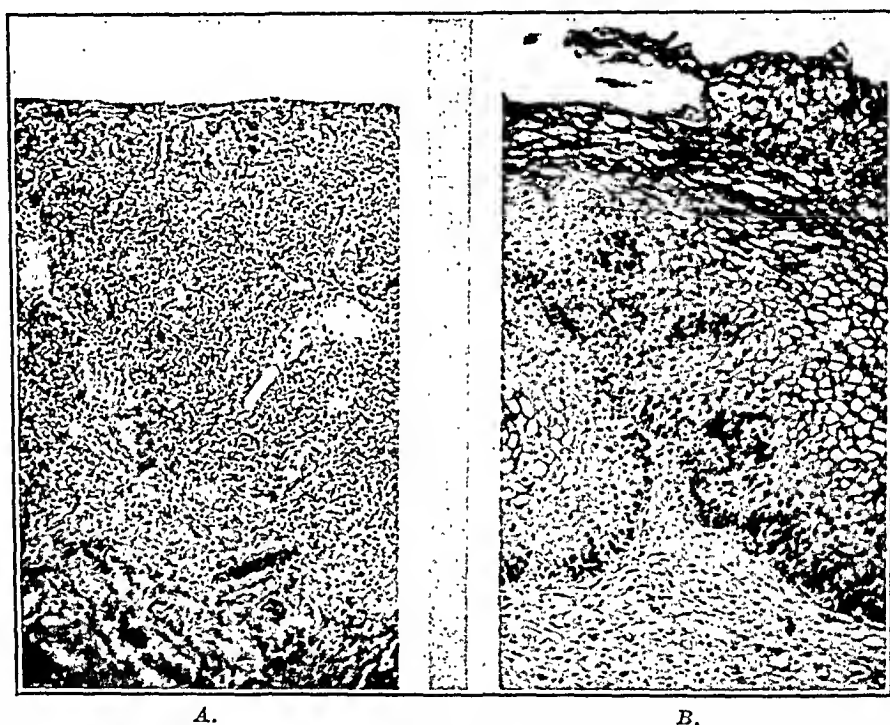


Fig. 7.—A, Case 29, before treatment. B, Case 29. Suppositories for twenty-five days, 1,875 units.

these figures with those of the oil hypodermic group in whom the number of days for epithelial shedding was 13.5, for a consistently negative smear 17.5, and for complete treatment 25.1. In other words, the time required for the action of the drug was practically the same whether administered hypodermically or by suppository. The number of units required for this activity, however, was almost twice as great for hypodermic administration as was required per vaginam. It was also our impression that the vaginal epithelial change was more marked when the drug was administered per vaginam (Fig. 7, A and B). The difference in the effect upon the breast tissue is also worthy of note. Practically all of the patients who received considerable quantities of amniotin hypo-

dermically showed a certain amount of breast hypertrophy, whereas none of the group receiving treatment by suppositories showed any breast change. The facts that less of the hormone was necessary to produce a cure, that the epithelial change was more pronounced, and that there was no breast change when the drug was administered vaginally, have led us to conclude that there is some local action which takes place, due to an increased concentration of the drug in the pelvic tissues.

There were five cases which recurred after suppository treatment which are recorded in Table VI.

TABLE VI. RECURRENCE AFTER SUPPOSITORY TREATMENT (5 CASES)

CASE	AGE	DAYS TREATED	RECURRED AFTER	DAYS SUBSEQUENTLY TREATED	NO. UNITS AMNIOTIN	DAYS FOR EPITHELIAL CHANGE	NEGATIVE SMEAR	RESULT WELL AFTER
21	9	21	4 mo.	18	1,350	9	9	2 weeks
25	7	20	14 days	59	4,425	23	37	2 weeks
29	5	25	10 days	16	1,200	8	8	2½ months
30	3	33	23 days	21	1,575	7	7	4 weeks
34	7	48	8 days	26	1,950	Persisted	12	2 weeks
Aver.	6.2	29.4	35 days	28.0	2,100	11.8	14.6	4 weeks

All of these five patients who had recurrences following the suppository treatment were promptly cured by retreatment with suppositories. It is interesting to note that the length of time required for epithelial change and negative smears was reduced when they were retreated, suggesting that perhaps some amniotin was still retained in the tissues. Inasmuch as the suppository group represents our most recent study, the length of time during which these recurrent cases have been well is necessarily short. The explanation of these recurrences offers certain difficulties, inasmuch as the children were not in an institution, and the question of reinfection must always be considered. In one instance, for example, we feel certain that this was the explanation for the patient who steadfastly denied sexual contact, returned with a primary syphilitic lesion as well as the gonococcal infection. In order not to mask results, we used no accessory treatment with the amniotin. It is possible that the percentage of recurrences may be reduced if irrigations are used in conjunction with the suppositories at the time of the epithelial shedding. Another procedure which may result in a greater percentage of permanent cures and which we intend to carry out in a subsequent series is to attempt to maintain the epithelial thickening over a longer period of time by the use of a suppository once or twice a week after the active treatment has been stopped.

TABLE VII. SUMMARY AND COMPARISON OF METHODS

METHOD OF TREATMENT	NO. PATIENTS TREATED	NO. PATIENTS WELL	PER CENT WELL	AVERAGE DAYS TREATED	AVERAGE NO. UNITS AMNIOTIN
Oral	6	1	16.6	123	191,600
Hypodermic E. G. preparation	10	1	10.0	19	950
Hypodermic oil preparation	22	16	72.2	27	4,206
Vaginal suppository	17	17	100	27	2,024

The table is self-explanatory and shows clearly the superiority of treatment by the suppository method. At present all of the thirty-five patients treated are well. Those who failed to respond to the oral or ethylene glycol hypodermic administration were subsequently cured by hypodermic oil administrations or vaginal suppositories. Patients who were resistant to the hypodermic oil preparation were promptly cured with suppositories.

One of the first and most essential requisites of any treatment is that it do no harm. During these experiments we were constantly on the lookout for any untoward effects. None were noted except some local reaction about the site of the hypodermic oil administrations. Considerable tender induration could often be felt and in one case a sterile abscess formed. It is our impression that the discomfort during and following the oil injection offers a distinct disadvantage to this method of treatment. There were no cases in the entire series in which there was any evidence of involvement of the upper genital tract. Rectal palpation of the internal pelvic organs showed no gross change. The question of any subsequent ill effect as the result of the hormonal action upon the genital tract must be considered. It was shown by the biopsies that the effect on the vaginal mucosa was very transient. Fig. 6, C shows the typical retrogression which had taken place on an average of four weeks after termination of treatment. Inasmuch as the vaginal mucosa is the most sensitive index of the action of the estrogenic hormone, it would seem likely that there remains no permanent effect upon the uterus or ovaries. That this is true is borne out by the work of Allen and Diddle<sup>5</sup> who gave monkeys doses of amniotin comparable to those used in the treatment of vaginitis. Examination of the monkey's ovaries thirty days after the cessation of treatment showed them to be histologically normal. H. B. Shumacher<sup>6</sup> working with mice came to exactly the same conclusions. Hence, judging by all clinical and laboratory criteria, it would appear that there is no evidence that the administration of the hormone is harmful.

## SUMMARY AND CONCLUSIONS

1. Amniotin administered orally or hypodermically in ethylene glycol solution is of no value in the treatment of gonococcal vaginitis. We have been unable to demonstrate any effect of the hormone on the vaginal mucosa or breasts.

2. Amniotin in oil has proved effective both in the production of maturation of the vaginal mucosa and in its therapeutic action in gonococcal vaginitis in 72 per cent of the cases. In most of the patients receiving prolonged treatment breast hypertrophy was noted.

3. Amniotin in suppository form has been proved to be effective in the production of mature vaginal epithelium and in its therapeutic effect in gonococcal vaginitis in all the cases in which we have used it. This group included some cases which had been resistant to the hormone when administered hypodermically in oil.

4. The epithelial change produced by the hormone, whether administered hypodermically or in suppositories, is transient, and there is no clinical or experimental evidence to show that its administration is harmful in dosage necessary to cure this disease.

5. So far as our experience has gone we have concluded that amniotin administered in suppository form is superior to any other known method of treating gonococcal vaginitis.

The authors wish to express their thanks to Dr. Edwards A. Park and the Pediatrics Staff for their cooperation in carrying out this study.

## REFERENCES

- (1) Report of a Project of the Bellevue-Yorkville Health Demonstration of New York City, by Walter M. Brunet, M.D., Dora M. Tolle, M.D., Sara Alicia Scudder, Anne Ruth Medealf. Reprinted from Hospital Social Service Magazine, Supplement No. 1, March, 1933. (2) Crossen, R. J.: J. Pediatrics 6: 82, 1935. (3) Allen, Edgar: Sex and Internal Secretions, Baltimore, 1932, Williams and Wilkins Co. (4) Lewis, R. M.: AM. J. OBST. & GYNEC. 26: 593, 1933. (5) Allen, E., and Diddle, A. W.: AM. J. OBST. & GYNEC. 29: 83, 1935. (6) Shumacher, H. B.: Personal communication. Nabarro, David: Lancet 228: 604, 1935. Miller, J. R.: AM. J. OBST. & GYNEC. 29: 553, 1935. Brown, Joseph: J. A. M. A. 102: 1293, 1934. Huberman, J., and Israeloff, H. H.: Ibid. 103: 18, 1934.

1201 NORTH CALVERT STREET

---

Fournier, R.: An Exceptional Secondary Accident After Spinal Anesthesia for Cesarean Section, Rev. franç. de gynéc. et d'obst. 30: 148, 1935.

The author reports a case in which after a spinal anesthesia for a cesarean section, a patient developed clonic, generalized convulsions followed by a period of coma. He points out that epileptic convulsions rarely occur after a spinal anesthetic. Forgue and Basset in their report of 1928 mention only two such cases which occurred among 130,000 spinal anesthetics. However, during the discussion of this paper, four other cases were mentioned. The author believes that two factors are involved in the production of convulsions after spinal anesthesia. The first is a disequilibrium in the tension of the cerebrospinal fluid, and the second is toxicity of the substance injected into the spinal canal.

J. P. GREENHILL.

## PROTEIN STABILIZATION IN PREECLAMPSIA AND ECLAMPSIA\*

BOYD HARDEN, M.D., W. S. McELROY, M.D., AND R. R. HUGGINS, M.D.,  
PITTSBURGH, PA.

*(From the Department of Obstetrics, School of Medicine, University of Pittsburgh)*

CERTAIN results of investigation of the toxemias of pregnancy, particularly preeclampsia and eclampsia, are presented herewith. The study was conducted at the Elizabeth Steel Magee Hospital from Jan. 7, 1922, to Sept. 1, 1933. During this period there were 24,533 ✓ deliveries, of which 139 were eclamptics, an incidence of 0.566 per cent. The eclamptic mortality was 21.5 per cent and these deaths constitute 9.36 per cent of the total maternal mortality.

Exercising the viewpoint that the logical solution of the problem lies in prevention rather than attempt at cure after eclampsia has developed, a special effort was made to correlate the clinical and laboratory findings in the hope of adding further to our knowledge of the fundamental factors contributing to the final picture of eclampsia. The plan of investigation included analysis of the history, clinical findings and course, as well as extensive laboratory study. Much of this assembled mass of clinical and laboratory data is in corroboration of previous observation. However, there are certain findings of special significance.

That we may not lose ourselves "in a maze of phantasies, revolving in idle circles," the discussion is presented in three divisions: (1) The changes in the maternal constitution incident to so-called physiologic gestation. (2) The outstanding clinical features of preeclampsia and eclampsia, and notes on treatment with reference to the clinical use of an alcoholic extract of liver known as heparmone. (3) The application of protein stabilization as a measure of study of preeclampsia and eclampsia.

### 1. CHANGES IN THE MATERNAL CONSTITUTION INCIDENT TO SO-CALLED PHYSIOLOGIC GESTATION

The maternal constitution undergoes profound changes in the course of so-called normal pregnancy. Increase in basal metabolic rate has been variously estimated from 4 to 30 per cent.<sup>22</sup> This increase in basal rate is proportional to the combined surface area of mother and fetus. The thyroid gland shows a definite hypertrophy which is a true hyperplasia, and the chromophile cells of the parathyroid bodies increase in number.<sup>22</sup>

\*This study was made possible by a grant from the Buhl Foundation of Pittsburgh, Pennsylvania.

The pituitary gland undergoes hypertrophy in its anterior lobe.<sup>22</sup> There is marked hypertrophy of the cortex of the adrenals.<sup>22</sup> Changes in the islet tissue of the pancreas have not, to our knowledge, been demonstrated. The ovaries show atresia of the follicles with hyperplasia of the inner layer of the theca.<sup>22</sup>

Haden<sup>3</sup> reports 4.2 million and Osgood<sup>13</sup> 4.8 million as the normal red count in the nongravid woman. Galloway<sup>2</sup> reports 3.8 million red cells and 71 per cent hemoglobin in the third trimester of normal pregnancy, which is associated with increase in blood volume according to Kapoth,<sup>22</sup> and a lowered specific gravity according to Lloyd-Jones and Zangemeister.<sup>22</sup> Strauss and Castle<sup>26</sup> have classified the anemias of pregnancy in three groups. The first group shows a progressive increase in anemia through the second trimester, which is followed by an abrupt rise in the third trimester. This group represents the so-called physiologic anemia of pregnancy. The second grouping shows a gestational hypoacidity and is called the hypochromic or chlorotic type. The third group exhibits complete posthistamine gastric anacidity. Strauss and Castle<sup>26</sup> have further shown that the blood picture of infants born of anemic mothers is identical with the blood of infants born of mothers showing no anemia.

Normal pregnancy is characterized by a positive balance of nitrogen, more marked in the latter half of gestation.<sup>4, 6, 10, 11, 14, 20, 21</sup> This positive nitrogen balance is due to the formation of tissue protein in the developing fetus rather than faulty elimination by kidney, since the nonprotein nitrogen of the blood is normal or slightly lowered and the urea fraction definitely below the average found in nonpregnant women. The total protein of the plasma tends to fall, gradually, after the third month, due chiefly to a reduction in the plasma albumin.<sup>22</sup> As a result a relative increase in globulin occurs.

Most observers agree that the level of blood stream sugar approximates normal in uncomplicated pregnancy.<sup>5, 9, 10, 23, 27</sup> There is, however, a frequent variation from the normal in the sugar tolerance curve, and a tendency toward acetonuria which becomes more pronounced when carbohydrates are withheld from the diet.

Gradually increasing from the third month of gestation, the latter part of normal pregnancy is marked by approximately a 30 per cent increase in blood stream fat.<sup>22</sup>

Normal pregnancy is accompanied by a lowering of alveolar CO<sub>2</sub> tension, by lowering of CO<sub>2</sub> combining power of the blood, and about a 5 per cent reduction in total fixed base. There is a slight lowering of calcium and phosphorus of the blood, decreased sodium concentration of the serum and increased sodium concentration of the corpuscles, while potassium and magnesium remain about the normal levels.<sup>1, 8, 12, 16, 17, 22</sup>

The significance of these changes in the maternal constitution in uncomplicated pregnancy is incompletely understood.

## 2. CLINICAL FEATURES OF PREECLAMPSIA AND ECLAMPSIA

In the analysis of any considerable number of cases of preeclampsia and eclampsia one is increasingly drawn toward the conclusion that a certain type of physical habitus is particularly predisposed to eclampsia,

that the incidence, severity, and mortality in this group rises with the demands of convention on the sensitive, illegitimate mother. In a term of brevity these individuals may be classified as a hypopituitary type with a normal or subnormal thyroid function. The influence of previous acute and chronic infections on the development of such constitutions is a deep but worthy problem. In the past three years no patient with preeclampsia has presented herself at our clinics who has failed to show an intercurrent acute infection, or an active focus of infection. Foci of infection, in the order of importance are: teeth, tonsils, cervix, sinuses, appendix, and gallbladder. Clinical improvement with the eradication of foci of infection has been the rule. Further, close inquiry into the dietary history reveals inadequacies, improprieties, and inability in the ingestion, digestion, and assimilation of foods. Strauss and Castle<sup>26</sup> have stressed these factors in relation to the anemias of pregnancy. In gestational toxemias controlled studies constitute a desirable adjuvant.

*Preeclampsia.*—The symptomatic gestational history of the eclamptic, in this series, shows a minimal duration of two weeks and a maximal duration of twenty-eight weeks. The findings in the early gestational toxemias cannot, at present, be utilized to predict the individual who will develop eclampsia. The individual who presents heartburn, scotomas, frontal headache, tinnitus, and formication and numbness of the extremities in the earlier weeks of gestation *often carries severe renal damage*, marked hypertension, and is destined to a premature termination of pregnancy or death.

Weakness and lassitude have been the dominant symptoms from the sixteenth to the twentieth weeks.

Headache appears in 86 per cent of the cases, after the twentieth week of gestation, and is usually frontal or occipital, infrequently bitemporal or sincipital. Transient blindness appears in 20 per cent of the series, and is associated with spasm of retinal vessels, edema of the optic discs, and occasionally with retinitis and retinal detachment. These eyeground changes are referable in but few cases to a known hypertension antedating pregnancy, or an established preexisting nephritis.

Dyspnea is a rather constant finding and is accompanied by precordial distress, positional vertigo, palpitation and anginal type of pain, a cardiac symptom complex probably referable to the same type of vasospastic change seen in the eyegrounds. Blood pressure shows a tendency to reversal of the normal diurnal rhythm with attainment of the higher levels during the night. A four-hour day and night average of blood pressure, in the antepartum period, is 170/105.5 mm. of Hg with the pulse pressure approximating one and one-half times the normal.

The appetite is variable in 23 per cent of the series, while 68 per cent show nausea and vomiting which may extend throughout the day. There

is a sense of weight in the epigastrium and regional soreness in the right upper quadrant, upon which is superimposed lancinating epigastric pain in 51 per cent of the cases. Pyrosis is usually associated and is worse after the evening meal. Residual gastric content shows lowered or absent free hydrochloric acid and lowering or absence of total acid. Total absence of acid is associated with a history of protracted vomiting or a clinical finding of profound anemia.

The frequency and urgency of a scanty and scalding dysuria require from four to thirty visits to the bathroom each night. The urine, barring alkalies for heartburn and high alkali residue diet, is acid, concentrated, and shows 860 to 38,600 mg. of quantitative protein in twenty-four hours.

Edema gradually becomes generalized and does not disappear with rest.

*Eclampsia.*—In this study one is impressed by the long periods of lavish physical torture which usually exist before the culmination of the tragedy of eclampsia. In more than 60 per cent of the patients, convulsions began between twelve noon and midnight. In the occasional case delivery witnessed the onset of convulsions, while about two-thirds as many convulsions occurred postpartum as the combined antepartum and intrapartum attacks. Of the 139 cases, six cases had a single convulsion. The greatest number of convulsions in one individual was thirty-one.

The preeclamptic symptoms and signs are for the most part accentuated in the eclamptic stage. Elevation of temperature is the rule, in this series reaching 99° to 104°. The skin may assume a peculiar lemon yellow to waxy tint. Cyanosis is usually pronounced and is frequently proportional to the amount of pulmonary edema which, in turn, may be referable to irregularities of rate, rhythm, and force of heart action. The average blood pressure in the eclamptic and intrapartum course is 181/110.1 mm. of Hg with pulse pressure remaining around one and one-half times the normal figure. Blood pressure falls rapidly after delivery, unless renal damage is severe and permanent. In two to twelve hours postpartum, blood pressure begins a secondary rise, which may approach or exceed the maximum pressure in the antepartum period. There is a gradual fall of pressure, over a period of ten to nineteen days, to stabilization around one figure. The average pressure at discharge from the hospital is 127/84.6 with a pulse pressure approximating the normal level.

There may be varying degrees of abdominal distention, rarely pronounced in the earlier stages of eclampsia. Gastric contents invariably contain blood, which probably accounts for the marked increase in the urea fraction of the stomach contents; free hydrochloric acid is usually decreased or absent.



During and immediately after a convulsion the uterus is usually boardlike and remains so from forty seconds to seven minutes. In addition to the uterine tonicity of the convulsive state there may be combined the rhythmic contractions of labor. Frequent convulsions and regular uterine contractions presage fetal death. Intrauterine fetal death is usually accompanied by varying periods of improvement in the clinical condition of the patient.

The urine becomes more concentrated, reddish brown to ashen in color, and decreases in amount, or there may be a total anuria from two to twelve hours. The urinary output varies from 0 to 90 c.c. an hour, the usual output varying from 2 to 30 c.c. an hour. The application of the vasospastic changes seen in the eyegrounds to the severe grades of renal difficulty is supported by the observation of Hinselmann and of Nevermann<sup>22</sup> that 60 per cent of all pregnant women show capillary spasm. Twenty-four-hour quantitative protein shows a variation from 1,945 to 23,219 mg. As the frequency, duration, and severity of convulsions decrease, there is a gradual increase in urine output. In a time interval of five hours, the output may rise from 1 to 2 c.c. an hour to 240 c.c. an hour. The usual improvement in urinary output in the first twelve hours postpartum is followed by a secondary decrease at the end of eighteen to thirty-six hours, which approximates the secondary rise in blood pressure. The urine is now alkaline, of high specific gravity usually, and straw to amber in color. The gradual subsidence in pressure, over ten to nineteen days postpartum, is marked by a gradual improvement in urinary output.

Anemia in preeclampsia and eclampsia is quite common. The average antepartum red cell count in preeclampsia and eclampsia is below the average figure for normal pregnancy and far below the average counts in the nongravid woman. Fifty-six cases of preeclampsia show an average red count of 3.4 million and 22 cases of eclampsia show an average of 3.6 million antepartum. These cases were not associated with hemorrhage or other accidents of labor. Further, the blood picture in the eclamptic is poorly maintained as compared to the preeclamptic. The average postpartum lowering of red cells in 26 cases of eclampsia is three times as great as in 29 cases of preeclampsia. Since faulty and inadequate diets, as well as disturbances in digestion, are factors which have been stressed in relation to the anemias of pregnancy, the quality and quantity of protein administered in preeclampsia assume particular importance.

The results on the chemical analysis of blood alone have largely confirmed the results of others in preeclampsia and eclampsia. The non-protein nitrogen, on the average, was a little higher than in normal pregnancy, due to varying degrees of renal involvement. However, there is a record of but one patient who presented a blood nonprotein nitrogen in the uremic levels. The blood urea was usually within the

limits of normal for the nonpregnant woman but above the average level of uncomplicated pregnancy. This is consonant with the non-protein nitrogen findings. Uric acid approximated twice the normal figure.  $\text{CO}_2$  combining power varied greatly, the limits of variation being 12 and 68, with a tendency for the figure to seek the acid levels. The calcium content of the blood was somewhat lowered, while inorganic phosphorus was distinctly elevated. Fatty acid content of the blood approximated a 50 per cent increase. Sugar, creatinine, chlorides, and cholesterol showed no marked variation from normal pregnancy, while serum proteins occasionally rested in edema levels.

These clinical and laboratory findings, for the most part, were accumulated in a period in which an alcoholic extract of liver, known as heparmone, was being applied in our clinics in preeclampsia and eclampsia. Sixty-seven cases treated with heparmone compared with sixty-six cases treated by various other measures gave the following results in eclampsia:

1. Heparmon had no sustained hypotensive effect antepartum, intrapartum, or postpartum.

2. Heparmon did not control the number, the interval, or duration of convulsive seizures, while its use was frequently accompanied by accentuation of headache, the development of pruritus and generalized subcuticular flushing.

3. Increase in visible edema, in the eclamptic stage, was the rule in the heparmon series.

4. Quantitative urinary proteins were higher in the heparmon series than under any other system of care. However, it is important to state that these results were obtained under a regime of strict enforcement of fluids.

The use of heparmon in the treatment of toxemias of pregnancy has been abandoned in our clinics.

### 3. APPLICATION OF PROTEIN STABILIZATION AS A MEASURE OF STUDY OF PREECLAMPSIA AND ECLAMPSIA

Our summaries emphasize two signal facts in preeclampsia and eclampsia:

1. The evidence of extensive vasospasm is visible in the eyegrounds, demonstrable in blood pressure readings, and is deductable from functional aberrations in brain, in heart, and in kidney.

2. Protein loss may reach surprising magnitudes, even when protein intake lies far below maintenance levels. The severe anemia seen in some of these cases may be referable to inadequate intake of blood-building materials, or to increased destruction of blood. The natural inference in treatment is the attempt to reduce constitutional strain and protect the body from the dissipation of vital protein. Bearing on this disturbance in protein metabolism, the following points are of interest:

1. In the course of normal pregnancy, especially in the latter months, protein should normally be retained to provide for the developing fetus. Therefore, a negative balance, at this time, would be of more serious import.

2. The increased permeability of the kidney to protein dissipation is responsible in part for the reduction of plasma proteins observed in preeclampsia.

3. The higher mortality appears in those cases presenting the greater protein dissipation without adequate replacement.

Extensive investigation of nitrogen balance was instituted in August, 1932. The measures adopted were designed to neutralize protein loss and bring the protein metabolism of the mother into better balance, or a state of stabilization. For purposes of comparison all cases were divided into two classes and placed on a standard regime. The conscious patients, able to cooperate, comprised the first group, while the second group contained those unable to cooperate, i.e., unconscious, or unable to retain food by mouth.

*Group One.*—The total caloric intake was adjusted to the twenty-four-hour resting requirement, using the DuBois chart as a guide. The protein requirement was calculated on the basal requirement, and was also determined from the total non-protein nitrogen of the urine, plus the urinary protein. For example, if the urine contained 10 gm. of nonprotein nitrogen, this, times the nitrogen factor for protein, 6.25, gave the equivalent amount of protein metabolized, or in the example  $6.25 \times 10 = 62.5$  gm. of protein. If the urine, in addition, contained 20 gm. of protein, (ordinarily considered as albumin), this was added to the protein metabolized, giving in the case  $62.5 + 20 = 82.5$  gm. of total protein metabolized and lost. The protein intake was adjusted to meet this requirement, the heavier meats being avoided. In addition, a high carbohydrate, low fat diet was employed, the ratio of carbohydrate being four to one of fat. This was adopted because of the well-known sparing action of carbohydrate on protein metabolism, and was an indirect attempt to reduce blood stream fat. Fluid was not restricted below 2,000 c.c. per day. Elimination was secured by the use of milk of magnesia or the daily use of soapsuds enemata. Morphine was used sparingly to control pain or restlessness.

*Group Two.*—These patients were placed on 10 to 25 per cent glucose by vein at four- to six-hour intervals, to the approximate twenty-four-hour caloric requirement. Conscious of the fact that protein dissipation could not be prevented by this measure, nevertheless the glucose supplies readily available energy and tends to minimize the destruction of tissue protein in the patient who is unconscious or unable to retain and assimilate foods by mouth. The lower bowel was emptied by colonic irrigation and a retention catheter, placed in the bladder, was released hourly. These patients were given sufficient morphine to bring the respiratory rate to twelve.

Fifteen referred cases of eclampsia and thirty-one cases of preeclampsia have been studied under this regime. It has not been possible, in this group, to establish nitrogen equilibrium but the nitrogen deficits have been compensated by estimating and feeding the quantitative amounts of protein required. By this simple procedure clinical symptomatology and signs have been much reduced, with the exception of the control of elevations of blood pressure, but the average level of hypertension has been lower. Improvement in anemia has been uniform, the average counts being above the general average of normal pregnancy. Renal function has shown about a 25 per cent increase in efficiency of elimination of fluid, with a distinct rise in urinary nonprotein nitrogen and an increase in the urea fraction of nonprotein nitrogen. The subsidence of hypertension and the return of urinary function to normal postpartum have been more rapid under protein stabilization than had been our previous experience. The eclamptic incidence in our wards has been

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.

HARDEN ET AL.: PREECLAMPSIA AND ECLAMPSIA

531

reduced to 0.04 per cent. We have had no case, under protein stabilization, develop convulsions, yet the premonitory evidences on admission to the hospital were alarming in all cases studied. Three cases of eclampsia, carrying low blood pressures but with marked symptomatology, have developed in our wards in the period of this study. The symptomatology was unfortunately minimized in the presence of comparatively low blood pressures and efforts in study were not instituted as early as they might have been.

TABLE I. BLOOD CHEMISTRIES. E. M., PREECLAMPSIA, DELIVERED ON 273RD DAY

	ANTEPARTUM 12 DAYS TEMPERATURE 97.4	INTRAPARTUM TEMPERATURE 98	POSTPARTUM 61 DAYS
Nonprotein nitrogen	20.0	26.0	27.0
Sugar	62.0	84.0	99.0
Urea	5.2	8.5	11.1
Uric acid	2.2	3.4	3.6
Creatinine	1.5	1.5	1.36
Chlorides	450.0	472.0	445.0
C O <sub>2</sub>	32.64	46.7	48.2
Calcium	9.8	10.15	9.7
Phosphorus	2.5	3.2	2.78
Serum albumin	4.2	4.0	3.79
Serum globulin	2.4	1.9	1.04
Fat	432.0	456.0	421.0
Cholesterol	132.0	205.0	225.0

*Blood Counts*

	ANTEPARTUM 15 DAYS	POSTPARTUM 13 DAYS
R. B. C.	4,000,000	3,860,000
W. B. C.	11,100	12,800
Hemoglobin	74%	71%
Polymorphonuclears	88%	84%

*Urine Chemistries*

12 DAYS ANTEPARTUM	TEMPERATURE 99 $\frac{1}{5}$
Total nitrogen 6.07 = 37.9375 gm. protein	
Nonprotein nitrogen 3.89 = 24.3125 gm. protein	
64% of total nitrogen	= Nonprotein nitrogen
29% of nonprotein nitrogen	= Urea
Protein loss	= 13.625 gm.
1 DAY ANTEPARTUM	TEMPERATURE 98
Total nitrogen 6.0 = 37.5 gm. protein	
Nonprotein nitrogen 5.34 = 33.375 gm. protein	
89% of total nitrogen	= Nonprotein nitrogen
58% of nonprotein nitrogen	= Urea
Protein loss	= 4.12 gm.

Our experience in this limited number of cases encourages a report on these results with the hope that others may find this method of approach useful in the study of preeclampsia and eclampsia. The most profound clinical alterations demonstrable in preeclampsia and eclampsia are in the field of protein metabolism: that this has a direct ap-

TABLE II. BLOOD CHEMISTRIES. ANTEPARTUM. E. S., ECLAMPSIA. NOT DELIVERED. INFANT LIVING. PATIENT SYMPTOMATICALLY FREE

	202ND DAY OF GESTATION TEMPERATURE 98.3	204TH DAY OF GESTATION TEMPERATURE 98.3
Nonprotein nitrogen	28.6	33.7
Sugar	115.0	78.0
Urea	14.3	13.8
Uric acid	4.2	4.0
Creatinine	1.33	1.37
Chlorides	514.0	459.0
C O <sub>2</sub>	19.71	52.7
Calcium	12.2	9.8
Phosphorus	2.8	2.78
Serum albumin	3.1	2.89
Serum globulin	2.0	1.12
Fat	580.0	500.0
Cholesterol	135.0	100.0
Ieterus index	9.0	.

*Blood Count*

	202ND DAY OF GESTATION
R. B. C.	4,000,000
W. B. C.	10,600
Hg	81%
Polymorphonuclears	86%
Lymphocytes	14%

*Urine Chemistries*

202ND DAY OF GESTATION	TEMPERATURE 98 $\frac{3}{4}$
Total nitrogen 10.49 = 65.25 gm. protein	
Nonprotein nitrogen 6.25 = 39.06 gm. protein	
65.25% of total nitrogen	= Nonprotein nitrogen
42.00% of nonprotein nitrogen	= Urea
Protein loss	= 26.1875 gm.
209TH DAY OF GESTATION	TEMPERATURE 98 $\frac{3}{4}$
Total nitrogen 9.47 = 59.1875 gm. protein	
Nonprotein nitrogen 5.64 = 35.2500 gm. protein	
59% of total nitrogen	= Nonprotein nitrogen
77% of nonprotein nitrogen	= Urea
Protein loss	= 13.9375 gm.
224TH DAY OF GESTATION	TEMPERATURE 98 $\frac{3}{4}$
Total nitrogen 4.24 = 26.500 gm. protein	
Nonprotein nitrogen 3.82 = 23.875 gm. protein	
90% of total nitrogen	= Nonprotein nitrogen
83% of nonprotein nitrogen	= Urea
Protein loss	= 2.625 gm.

plication in the final outcome is more than probable. Any plan of prevention and treatment must take into consideration such measures as will tend to maintain the protein of the mother within the limits of normal pregnancy. Our findings have been such in this study that we propose to direct our efforts along this line in a further investigation of preeclampsia and eclampsia.

Grateful acknowledgment is made to F. B. Utley and F. W. Donley of the Department of Medicine, Mortimer Cohen of the Department of Pathology, J. S. Plumer of the Department of Ophthalmology, and T. B. McCollough of the Department of Otolaryngology, for their assistance in this report.

## REFERENCES

- (1) Denis, W., and King, E. L.: AM. J. OBST. & GYNEC. 7: 253, 1924. (2) Galloway, C. E.: AM. J. OBST. & GYNEC. 1: 84, 1929. (3) Haden, R. L.: Arch. Int. Med. 31: 766, 1923. (4) Harding, V. J., Allin, K. D., and Van Wyck, H. B.: J. Obst. & Gynec. Brit. Emp. 31: 595, 1924. (5) Hellmuth, K.: Klin. Wehnschr. 1: 1152, 1922. (6) Hellmuth, K.: Arch. f. Gynäk. 118: 18, 1923. (7) Hermann, E., and Neumann, J.: Biochem. J. 43: 47, 1912. (8) Krebs, O. S. and Briggs, A. P.: AM. J. OBST. & GYNEC. 5: 67, 1923. (9) Krebs, O. S., and Briggs, A. P.: Hospitalstid., Copenhagen 68: 1039, 1925. (10) Martin, C. H., and Robison, R.: Biochem. J. 16: 407, 1922. (11) McEllroy, W. S., and Pollock, H. O.: J. Biol. Chem. 46: 475, 1921. (12) Oard, H. C., and Peters, J. P.: J. Biol. Chem. 81: 9, 1929. (13) Osgood, E. E., and Haskins, H. D.: Arch. Int. Med. 39: 643, 1927. (14) Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry. Interpretations, Baltimore, 1932, Williams and Wilkins Co., pp. 267 and 268. (15) Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry. Interpretations, Baltimore, 1932, Williams and Wilkins Co., p. 336. (16) Plass, E. D., and Bogert, L. J.: Bull. Johns Hopkins Hosp. 35: 361, 1924. (17) Plass, E. D., and Matthew, C. W.: AM. J. OBST. & GYNEC. 12: 346, 1926. (18) Pribram, E. E.: Arch. f. Gynäk. 119: 57, 1923. (19) Sansum, W. D., and Woodyatt, R. T.: J. Biol. Chem. 30: 155, 1917. (20) Sherman, H. C.: J. Biol. Chem. 41: 97, 1920. (21) Smith, M.: J. Biol. Chem. 68: 15, 1926. (22) Stander, H. J.: Monographs in Gynecology and Obstetrics by Karl Henry Davis, Hagerstown, Maryland, W. F. Pryor, 1934 1: chap. 8. (23) Stander, H. J., Duncan, E. E., and Sisson, W. E.: Bull. Johns Hopkins Hosp. 36: 411, 1925. (24) Stander, H. J., Eastman, N. J., Harrison, E. P. H., Jr., and Cadden, J. T.: J. Biol. Chem. 85: 233, 1929. (25) Stander, H. J., and Radelet, A. H.: Bull. Johns Hopkins Hosp. 38: 423, 1926. (26) Strauss, M. B., and Castle, W. B.: Am. J. M. Sc. 185: 539, 1933. (27) Tisdall, F. F., Drake, T. G. H., and Brown, A.: Am. J. Dis. Child. 32: 854, 1926. (28) Van Slyke, D. D., Stillman, E., Moeller, E., Ehrlich, W., McIntosh, J. F., Leiter, L., MacKay, E. M., Hannon, R. R., Moore, N. S., and Johnson, C.: Medicine 9: 257, 1930. (29) Widdows, S. T.: Biochem. J. 17: 34, 1923. (30) Williams, J. L.: J. A. M. A. 76: 1297, 1912. (31) Zange-meister, W.: Ztschr. f. Geburtsh. u. Gynäk. 99: 92, 1903.

---

David-Chaussé, R.: Pruritus Vulvae. Etiologic and Therapeutic Consideration, Rev. franç. de gynéc et d'obst. 29: 1014 1934.

For the treatment of pruritus vulvae the author varies medication depending upon the etiology of the condition. For itching due to mycosis he prescribes a special preparation and he lists other drugs for pruritus due to microbial infection, diabetes and other causes. In cases where the etiology is unknown he applies symptomatic treatment. He has not employed radium therapy but believes that x-ray treatments in small doses are often helpful. He has tried the epidural injection route of auto-hemotherapy and autoserotherapy without any success. On the other hand, the intravenous injection of bromides has given relief. The injection of physiologic serum has not given constant results. Endocrine therapy has produced no favorable effects. For severe cases which resist all treatment surgical intervention is necessary. The various forms proposed are vulvectomy, resection of the presacral nerve, periarterial sympathectomy and bilateral chordotomy. The author believes that in most intractable cases of pruritus vulvae we should search for cellulitis of the pelvis.

J. P. GREENHILL.

## THE TREATMENT OF DYSMENORRHEA BY PRESACRAL SYMPATHECTOMY

FLOYD E. KEENE, M.D., PHILADELPHIA, PA.

TEN years ago, Cotte suggested presacral sympathectomy for the relief of pelvic pain, the chief indication being dysmenorrhea. Since then, he has contributed extensively to the subject and numerous publications from other clinics have accumulated in foreign literature, duplicating the excellent results which Cotte has reported. In striking contrast is the paucity of contributions by surgeons in this country. The results of this procedure in the treatment of dysmenorrhea have been reported by Adson and Masson, Counsellor and Craig, DeCourey, and Wetherell; its value in relieving pain associated with pelvic cancer has been discussed by Behney, and Greenhill and Schmitz. Although the number of patients so treated by each author is small, there is a unanimity of opinion that excision of the presacral nerve is a valuable addition to our therapeutic armamentarium, in that it often affords relief when other methods have failed.

For obvious reasons, presacral sympathectomy for dysmenorrhea is limited in its field of usefulness to young women, hence its value must be judged not only in terms of relieving pain but also by its effects on menstruation and pregnancy. Further, this operation severs the chief sympathetic nerve supply to the bladder and rectum as well as the uterus, and a satisfactory result must include unimpaired function of these organs. The purpose of this paper is to discuss the function of the presacral nerve so far as it bears upon these facts, to review briefly the anatomy necessary to the execution of presacral resection, and to report the results of this operation in seven cases of dysmenorrhea.

### AUTONOMIC NERVE SUPPLY OF THE PELVIC ORGANS

The nervous mechanism which regulates visceral function and other involuntary activities of the body has been designated by Langley as the autonomic nervous system. Composing this system are two groups of nerves, the sympathetic and the parasympathetic, which are antagonistic in their action and whose delicately adjusted coordination or balance is reflected in the normal function of the organs they supply.

The presacral nerve is that segment of the abdominal sympathetic system which extends from the bifurcation of the aorta to the sacral promontory. The term "presacral" which was chosen by Laterjet is anatomically incorrect, since the position is prelumbar and the conforma-

tion is usually that of a plexus rather than a true nerve. More appropriate is superior hypogastric plexus (Hovelacque) or prelumbar plexus (Elaut). This nerve is formed by the union of three roots. The lateral roots are composed of branches from the first and second lumbar ganglia and fibers which have taken their origin from ganglia in the region of the renal arteries. These nerve bundles pass downward to unite with the middle root which is a continuation of the intermesenteric plexus. Thus formed, the nerve is joined by fibers from the third and fourth lumbar ganglia on each side and after crossing the promontory of the

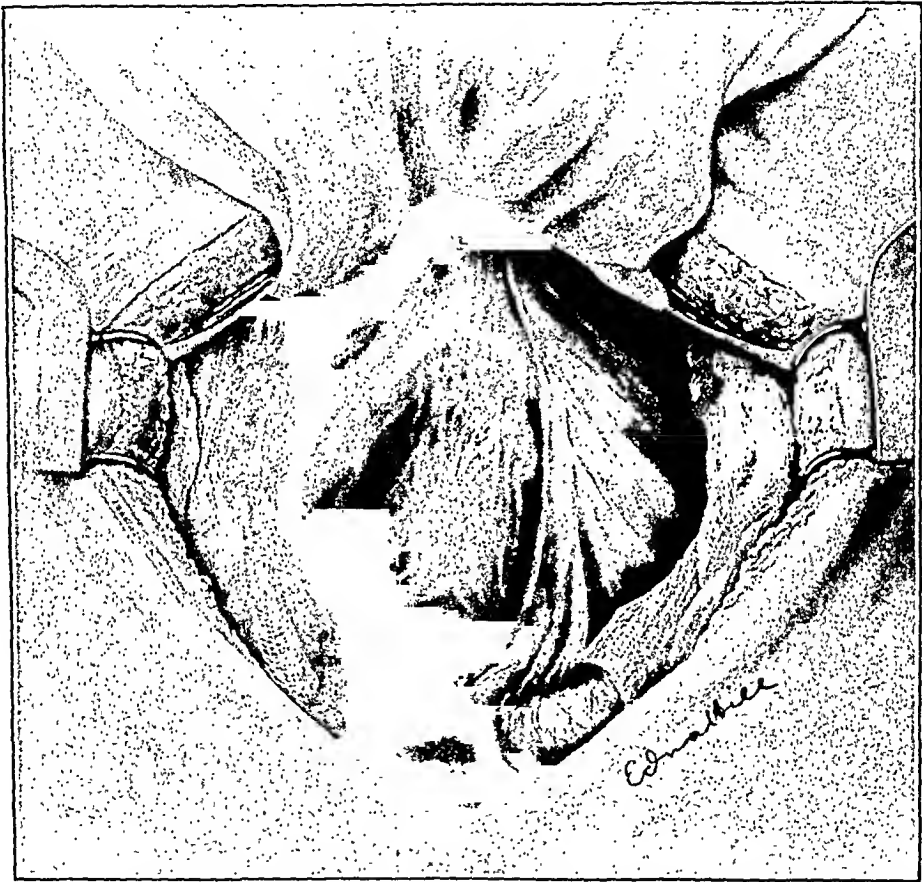


Fig. 1.—Interiliac space exposed. Note inferior mesenteric artery on the left. Presacral and inferior hypogastric nerves not usually visible through peritoneum but are depicted here to show relations of the nerve as well as its usual plexiform arrangement.

sacrum, it divides into the right and left hypogastric nerves. These nerves course along the posterior pelvic wall supplying branches to the ureters and enter the lateral rectal space, terminating in the inferior hypogastric ganglia. Here they are joined by the parasympathetics through the pelvic nerves (*nervi erigentes*) which are branches of the second, third, and fourth sacral nerves. Emerging from the ganglia, the combined fibers form a plexus anterior to the rectum in the region of the uterosacral ligaments and continue along the internal iliac artery and its branches to supply the genital organs, including the vagina, the



bladder, and the lower portion of the rectum. The sympathetic and parasympathetic nerves contain both efferent and afferent fibers, the latter reaching the spinal cord by way of a detour to the posterior roots.

The main sympathetic nerve supply of the ovary arises in the ovarian plexus and passes downward with the ovarian vessels to the infundibulopelvic ligament where it divides into two branches, one entering the ovary and the other the fallopian tube. A few fibers from the tubal division pass directly to the uterus and others anastomose with the plexus in the broad ligament.

*Anatomic Relations of the Presacral Nerve.*—The presacral nerve lies in what is called by Elaut the interiliae space which is in the form of a triangle with the bifurcation of the aorta as its tip, the common iliac arteries its lateral boundaries, and its base a line across the promontory of the sacrum. On the left side of this space is the inferior mesenteric artery coursing through the base of the mesocolon. Ordinarily this can be displaced to the left, but the root of the mesocolon may extend across the median line of the triangle, making access to the nerve not only difficult but also hazardous. Covering the interiliae space is the posterior parietal peritoneum through which, in thin subjects, the fibers of the nerves may be seen. Immediately beneath the peritoneum, or separated from it by more or less fat, is a sheet of fibrous tissue in which lies the presacral nerve usually in the form of a plexus rather than a single nerve. The plexus in its sheath crosses but is easily separated from the left common iliac vein which is seen as a broad band filling in the upper portion and left side of the triangle. As the nerve approaches the base of the triangle, it lies on the median sacral vessels and the prevertebral fascia covering the last intervertebral disc and fifth lumbar vertebra.

*Function of the Presacral Nerve.*—According to Gask and Ross, our understanding of the human sympathetic nervous system is very imperfect, for clinical experience not only reveals gaps in our knowledge but also casts doubt upon many current beliefs. One is forcibly impressed with the truth of this statement in reviewing the literature dealing with the physiology of the pelvic autonomic nervous system, since an array of conflicting opinions is encountered which warrants the conclusion of Davis that the indication for excision of the presacral nerve must necessarily rest upon a very insecure foundation. However, this foundation becomes more secure when it is realized that many of the opinions expressed are based upon animal experimentation and that with the advent of surgery during the past decade, our knowledge has been enhanced by clinical investigation and observation. Opinions may differ as to the influence exerted by the presacral nerve on a given organ, but we do possess a fairly accurate idea of the effect resection of the nerve will have upon the functional activity of that organ, which is of prime importance to the clinician and pertinent to the subject under discussion. To this end we shall summarize the opinions expressed in a few of the more recent contributions.

*Transmission of the Pain Impulses.*—Gask and Ross state that most if not all of the afferent fibers from the uterus travel in the sympathetic nerves to the spinal cord. According to Fontaine and Hermann, the hypogastric plexus carry the important pathways of sensation from the internal genital organs to the medullary centers. Similar evidence is found in the contributions of Kuntz, Cotte, Leriche, and Learmonth. Adson and Masson agree that presacral fibers undoubtedly carry sensations of pain but in their opinion, the relief of pain in functional dysmenorrhea is obtained not only by cutting the pain fibers but also from interruption of efferent fibers which supply the blood vessels in the genitalia and musculature of the uterus. Davis states that the relief of pain which follows resection of the presacral nerve is probably the result of vasomotor rather than any sensory function, but the absence of sensory fibers is by no means certain. There can be no doubt as to the efficacy of presacral nerve excision in relieving pain in the organs supplied by it, and what appears as incontrovertible evidence warrants the conclusion that the relief is in large measure ascribable to the division of sensory pathways, vasomotor changes being only secondary factors.

*Control of Uterine Function.*—The part played by the sympathetic and parasympathetic nerves in regulating the motor function of the uterus is unknown. To the conflicting opinions regarding the motor and inhibitory influence of these nerves is added evidence that uterine contraction occurs in the absence of nerve stimulation. In proof of this, is the frequently quoted experiment of Rein which shows that spontaneous birth of young in rabbits occurs after section of all extrinsic nerves of the uterus. Cotte refers to the demonstration of Calliburse, who extirpated the uterus from an animal in labor, suspended it in Locke's solution, and observed that contractions continued until fetal expulsion was completed. Of greater value is the clinical evidence pertaining to the regulation of uterine motor function by the nervous system. As to the parasympathetic influence, Fontaine and Hermann cite the observations of Mueller, Brachet, and Gertsman who have found that neither the section nor the complete destruction of the sacral part of the spinal cord will prevent childbirth, and Kuntz states that under these circumstances, parturition proceeds with abnormal rapidity. Of vital importance to the subject under discussion is the effect of sympathetic ablation upon subsequent pregnancy. Cotte states that in thirty pregnancies after presacral excision he has never observed any evidence of altered uterine contractility. He also reports two patients who were subjected to this operation during the early months of pregnancy on account of severe uterine pain. In both, the pain was relieved, pregnancy was uninterrupted, and they were delivered normally at term. Precipitate delivery in a nullipara forty-two years of age is reported by Davis who suggests that it provides some support of the view that the

presacral nerve is an inhibitor and the parasympathetic an excitor of uterine contraction. The only case of full-term pregnancy after presacral excision reported in this country is that of Wetherell. This patient was a nullipara who became pregnant a year and a half after operation. The first stage of labor lasted eighteen hours, the second stage four hours, and delivery was by midforceps because of posterior position of the occiput. The pains were irregular and weak, being in the nature of a backache with no pain in front. Her puerperium was uneventful. Although the exact control of the motility of the uterus is unknown, the consensus of opinion is that presacral sympathectomy does not interfere with parturition.

Ovarian function and the response of the uterus to this function are not directly subject to nervous regulation; the part played by the pelvic nervous system in menstruation has to do in large measure, if not entirely, with its influence on the blood vessels of the genital organs. Resection of the presacral nerve does not alter the normal rhythm of menstruation, but bleeding a few days after the operation and increase in the quantity and duration of the menstrual flow may result from removal of the constrictor influence exerted by the sympathetics upon the blood vessels of the uterus and broad ligaments.

*Control of Bladder Function.*—My remarks on the nervous mechanism concerned in the control of the bladder function are based upon the clinical investigations of Learmonth, who has made valuable contributions to the subject during recent years. Entering into this mechanism are three pathways, the sympathetic, the parasympathetic, and the pudic nerves. The sympathetics (presacral nerves) are inhibitory to the detrusor muscles and motor to the internal sphincter, trigone, and the ureteral orifices; they also exert a constrictor influence upon the blood vessels of the bladder. The parasympathetics (pelvic nerves) are motor to the detrusor muscles and inhibitory to the internal sphincter. The pudic nerves supply motor fibers to the compressor urethrae muscle and sensory fibers to the posterior urethra and internal sphincter. Normal micturition is dependent upon the integrity of the parasympathetic pathways which are unaffected by division of the presacral nerve. However, this nerve does stimulate sphincteric contraction and Learmonth's cystoscopic studies show that immediately after presacral excision, the sphincter, trigone, and ureteral orifices are relaxed. Within three weeks, this relaxation has disappeared, and he believes that the ability of the sphincter to remain closed after ablation of the motor influence is due to an inherent tonus which normally is merely reinforced by the sympathetic supply. Also of importance in its bearing upon presacral sympathectomy is the transmission of sensory impulses from the bladder. The sensation of fullness which is translated into a desire to urinate is transmitted by the afferent fibers of the parasympathetic (pelvic)

nerves; also along this pathway travel thermal and tactile impulses. Painful sensations due to an overdistended bladder or disease are transmitted by way of the sympathetic (presacral) nerves.

Clinical application of these facts is found in the use of presacral sympathectomy in the treatment of cord bladder as suggested by Learmonth and Braasch, of neurogenic dilatation of the ureters and of certain types of vesical pain. They also explain the absence of bladder impairment after excision of the presacral nerve.

*Control of Rectal Function.*—The sympathetic nerves which are blocked by presacral excision supply the lower rectum and the internal sphincter of the anus, the external sphincter, which is composed of voluntary muscle, being supplied by the inferior hemorrhoidal branches of the pudic nerves. The influence of the sympathetic and parasympathetic nerves on the rectum as well as the internal sphincter is similar to that exerted on the bladder, the one being inhibitory to the musculature of the rectal wall, and motor to the sphincter, the other exerting opposite effects. The ability of the internal sphincter to remain closed after section of its motor nerve supply may be explained in the same manner as Learmonth has applied to the vesical sphincter. As a further safeguard against incontinence is the external sphincter with its separate nerve supply. Further, as Kuntz states, both sphincters are normally in tonus, the force of tonic contraction of the external sphincter being greater than that of the internal. An abundance of clinical evidence shows that excision of the presacral nerve does not impair rectal function, in fact obstinate constipation may be relieved by it.

*Selection of Cases.*—The type of functional dysmenorrhea which responds most favorably to presacral excision is that in which the pain is located in regions corresponding to the final distribution of the presacral nerve. To this type, Cotte has applied the term hypogastric plexalgia in the belief that the pain is due to a dysfunction or actual disease of the nerves which compose the plexus. The spasmodic pain comes on a few days before or with the onset of the flow, and its point of maximum intensity is in the uterus, radiating to the sacrum or coccyx and often accompanied by bladder irritability. Cotte emphasizes the importance of differentiating this type of dysmenorrhea from that indicating involvement of the ovarian sympathetic plexus in which the pain is located in one or both sides of the pelvis, radiating to the lumbar region. Under these circumstances, the prognosis of relief from presacral sympathectomy is less favorable. For this type of pain, denervation of the ovaries by excision of the nerves in the infundibulopelvic ligament or by section of the ligament has been suggested; the former procedure would seem to present insuperable technical difficulties, and interference with the ovarian blood supply is a formidable objection to the latter.

Cotte presents convincing evidence to prove the value of presacral sympathectomy as a supplementary procedure to operations on the pelvic organs for organic lesions which may contribute to the dysmenorrhea. In a series of 200 cases, correction of the pelvic defects with presacral nerve excision gave a greater incidence of relief than in a similar group in which excision of the nerve was omitted.

*Technic of Operation.*—Through a lower midline incision extending to the umbilicus, the field of operation is exposed by packing the small intestines upward and to the right and retracting the sigmoid to the

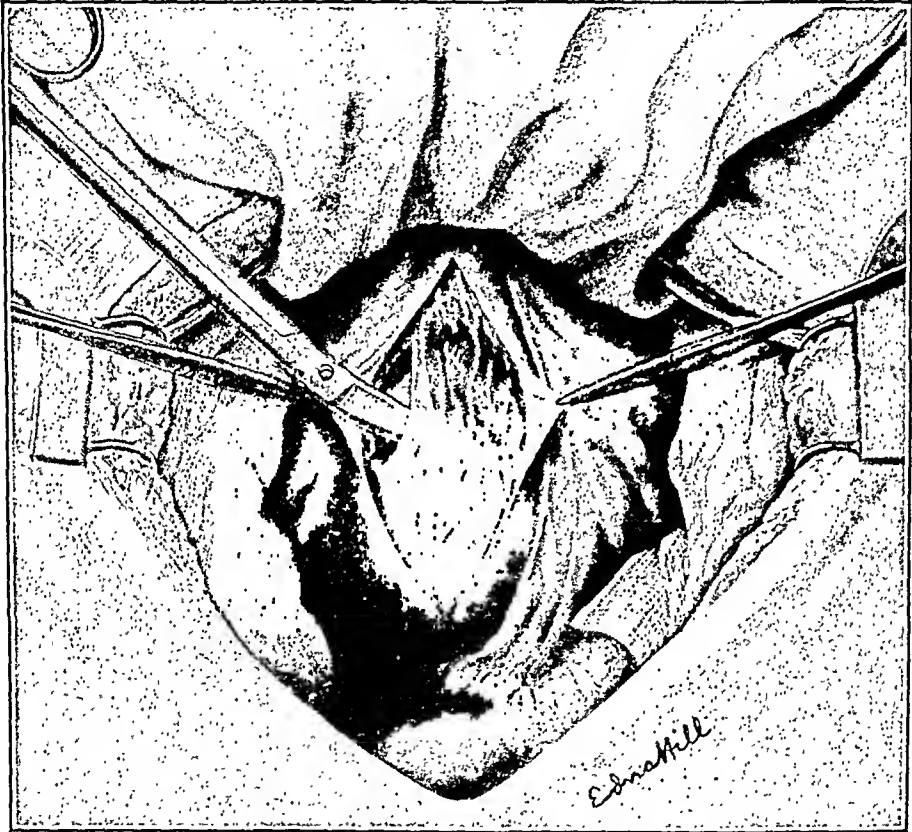


Fig. 2.—Beginning resection of fibrous sheath and nerve over right common iliac artery.

left. The landmarks thus exposed are the bifurcation of the aorta, the common iliac arteries, and the promontory of the sacrum. On the left side of this space is the inferior mesenteric artery coursing through the base of the mesocolon. The root of the mesocolon may extend across the interiliac space, overlying the presacral nerve. Under these circumstances, the peritoneal incision is made well to the right of the midline and exposure of the nerve beneath the thick, vascular mass is a difficult as well as hazardous procedure. Ordinarily, the posterior parietal peritoneum is incised in the midline just above the sacral promontory, and the incision is continued upward to the bifurcation of the aorta and downward over the promontory. The flaps of peritoneum are elevated

by blunt dissection as far as the common iliac arteries, exposing a sheet of fibrous tissue covered by more or less fat. This sheet of tissue contains the fibers of the presacral nerve. In thin subjects, the fibers can be seen and felt, but a thick layer of subperitoneal fat complicates the situation, making recognition and excision of the nerves more difficult. The separation of the sheath and nerve is made en masse, beginning over the right common iliac artery near the bifurcation of the aorta. By gentle blunt dissection, the separation is continued over the left iliac vein to the left common iliac artery. As Cotte states, the tissue surrounding the nerves in this area is very delicate, and its tensile strength is supplied by the nerve fibers which it contains. The sheet of tissue

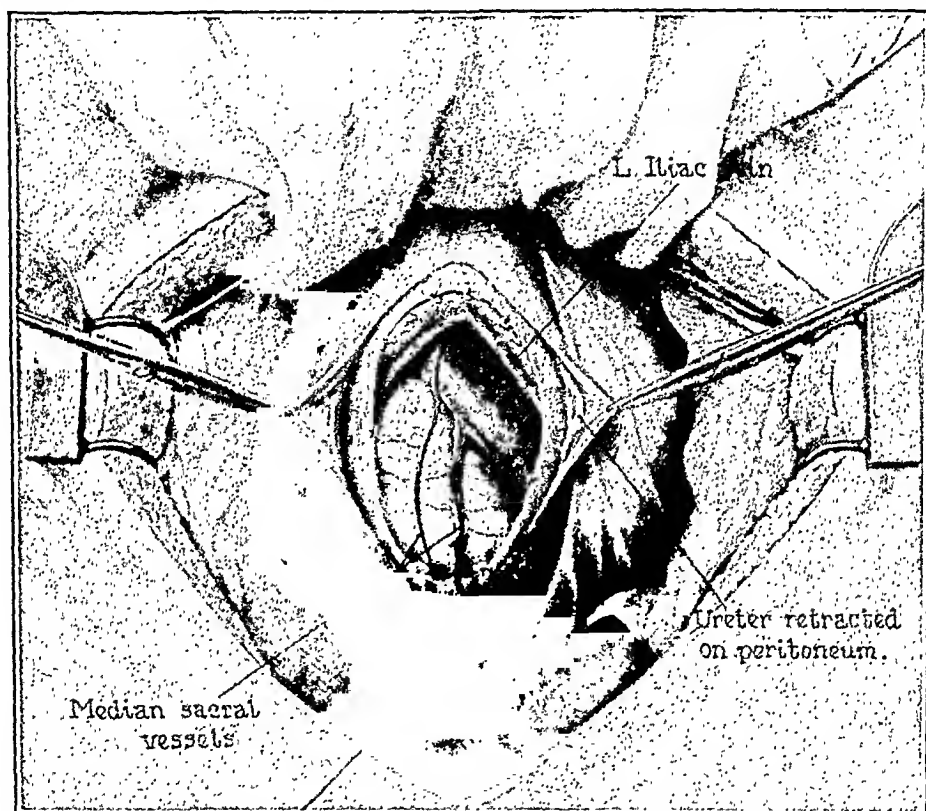


Fig. 3.—Operation completed, showing extent of resection and structures occupying interiliac triangle.

thus liberated is elevated and the dissection is carried downward, avoiding the median sacral vessels, until the division into the hypogastric nerves is recognized. The upper and lower attachments are severed after ligation with fine, plain catgut to avoid troublesome oozing from the vasa nervorum and the incision in the posterior parietal peritoneum is closed with a continuous suture.

*Report of Cases.\**—This report summarizes the results of presacral sympathectomy in seven cases of severe, intractable dysmenorrhea. In

\*My associate, Dr. Charles A. Behney, was among the first in this country to employ presacral sympathectomy for the relief of pelvic pain, and my adoption of the procedure is due in large measure to his influence. For his valuable assistance, I am deeply indebted.

five, the dysmenorrhea was of the functional type, the pelvic organs being normal with the exception of one who had been subjected to a left salpingo-oophorectomy. Extensive endometrial transplants in the culdesac and on the posterior surface of the broad ligament were present in one patient, and in another, the small, acutely anteфлекed uterus was retrocessed. In this last patient, the uterus was suspended and the appendix removed; in the remainder, presacral sympathectomy was the only operation performed.

With the exception of dribbling of urine in one patient for a few days after operation, the immediate convalescence differed in no respect from that of the ordinary laparotomy. As to the remote results, the menstrual rhythm has shown no alteration. In one the quantity and duration of the flow have increased slightly, and in another there has been a diminution. In none has there been impairment of bladder or rectal function. The results as regards relief of pain are summarized as follows:

CASE 1.—Patient aged twenty-four years, married, nullipara, operation Feb. 15, 1934. Pelvic organs normal. Before operation, the patient had pelvic discomfort with attacks of severe colicky pain for eighteen days prior to and during the periods. Now pain is present only during the period and is just as severe as before operation.

CASE 2.—Patient aged twenty-three years, married, nullipara, operation May 17, 1934. The patient had extensive endometrial transplants in the culdesac and on the posterior surface of the broad ligaments. The uterus was retroverted and the ovaries were normal. The extent of involvement and the history of great increase in severity of the dysmenorrhea during the year preceding the operation leave no doubt as to the part played by the lesion in the production of pain. The pain has been entirely relieved by presacral sympathectomy.

CASE 3.—Patient aged twenty years, single, operation June 29, 1934. Pelvic organs normal. No relief from dilatation of the cervix and Baldwin drain. Since presacral excision, only slight discomfort during the first few hours of the period.

CASE 4.—Patient aged thirty-two years, married, nullipara, operation Sept. 18, 1934. Uterus small, acutely anteфлекed, and retrocessed. Ovaries normal. Suspension of uterus and appendectomy in addition to presacral sympathectomy. Pain entirely relieved.

CASE 5.—Patient aged twenty-two years, single, operation Oct. 30, 1934. Pelvic organs normal. Root of mesocolon displaced to right, making exposure of nerve difficult. Only slight relief of pain during the first two periods after operation. Since then pain has decreased so that now it is controlled by mild sedatives and patient is no longer incapacitated from work.

CASE 6.—Patient aged twenty years, married, nullipara, operation Nov. 14, 1934. Left salpingo-oophorectomy had been performed a year previously with no relief. The right adnexa and uterus were normal. She now has a "heavy feeling in the abdomen" and slight pain during the first day of the flow. Menstrual and intermenstrual backache persists.

CASE 7.—Patient aged twenty years, single, operation Nov. 27, 1934. Pelvic organs normal. Exposure of nerve complicated by displacement of mesocolon to the right.

Central, colicky dysmenorrhea has been entirely relieved by operation. During the four subsequent periods, she had bilateral pelvic pain of moderate severity, and the last two periods have been practically painless.

### CONCLUSIONS

1. This experience, combined with that of others reported in the literature, justifies the belief that presacral sympathectomy has a place in the treatment of properly selected cases of functional dysmenorrhea, but its adoption is warranted only when less radical measures have failed.

2. In organic dysmenorrhea, presacral sympathectomy may be used with advantage to supplement operations on the pelvic organs.

3. Ordinarily, the operation is not difficult, but conditions may be encountered rendering its performance not only tedious but also hazardous.

4. The operation relieves pain in the majority of cases and does not interfere with menstruation, spontaneous parturition, or motor control of the bladder and rectum.

### REFERENCES

- Adson, A. W., and Masson, J. C.: J. A. M. A. 102: 986, 1934. Bchney, C. A.: Ann. Surg. 101: 411, 1935. Cotte, G., and Dechaume, M.: J. de Chir. 25: 653, 1925. Cotte, G.: Chirurgie du sympathique pelvien en gynecologie, Paris, Masson, 1932. Cotte, G.: Zentralbl. f. Gynäk. 57: 1, 1933. Counsellor, V. S., and Craig, W. McK.: AM. J. OBST. & GYNEC. 28: 161, 1934. Davis, A. A.: Brit. M. J. 2: 1, 1934. DeCourcy, J. L.: Am. J. Surg. 23: 408, 1934. Fontaine, R., and Hermann, L. G.: Surg. Gynec. Obst. 54: 133, 1932. Gask, G. E., and Ross, J. P.: Surgery of the Sympathetic Nervous System, Baltimore, 1934, William Wood and Company. Greenhill, J. P., and Schmitz, H. E.: J. A. M. A. 101: 26, 1933. Kuntz, A.: The Autonomic Nervous System, Ed. 2, Philadelphia, 1934, Lea and Febiger. Learmonth, J. R., and Braasch, W. E.: Surg. Gynec. Obst. 51: 494, 1930. Learmonth, J. R.: Brain 54: 147, 1931. Leriche, R., and Fontaine, R.: Presse méd. 34: 1121, 1926. Rein, G.: Soc. de Biol. 1882. Wetherell, F. S.: AM. J. OBST. & GYNEC. 29: 334, 1935.

---

Klaften, E.: Theory and Results of Vaginal Insulin Treatment of Cervical Erosions, Med. Klin. 31: 44, 1935.

During the last year Klaften has treated a large number of cervical erosions regardless of their etiology by means of intravaginal applications of insulin. This treatment has yielded excellent results. He observed that it delayed menstruation between two and nine days but he never noted any symptoms of hypoglycemia following the treatment. Even though there is some absorption of the insulin placed in the vagina, this form of therapy cannot be employed for diabetes. The good effects obtained in cases of cervical erosion are the result of local action and not of the absorbed insulin. Of course, one must be certain that the area to be treated is not a carcinoma.

Good results followed insulin application both in the form of a solution and as tablets. Both forms of therapy affected the ovaries as evidenced by the delays in menstruation. Hypodermic injections of insulin act in the same way on the ovaries but in a much more pronounced form.

J. P. GREENHILL.



# THE PLACE OF COLPECTOMY IN THE TREATMENT OF UTERINE AND VAGINAL PROLAPSE

LOUIS E. PHANEUF, M.D., Sc.D. (HON.), BOSTON, MASS.

THE term prolapse, when used in a general sense, denotes the descent of the uterus, bladder, urethra, rectum, and occasionally the culdesac of Douglas, through the vaginal introitus. When used in a limited sense, prolapse may refer to the extrusion of individual organs such as the

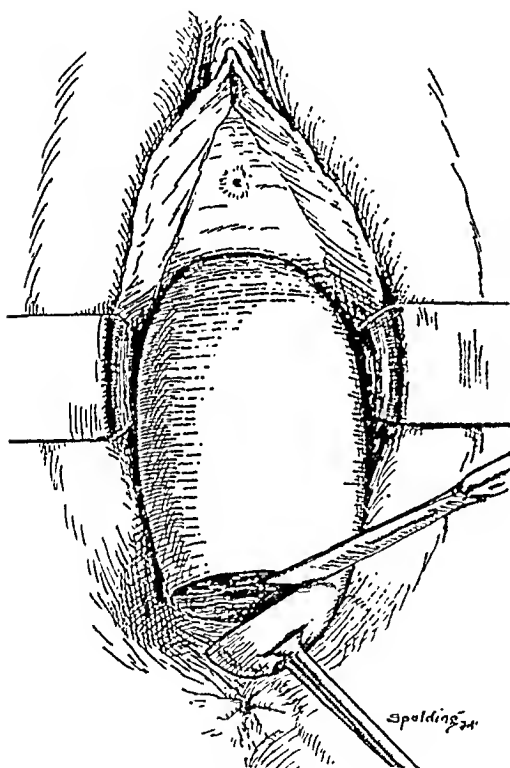


Fig. 1.

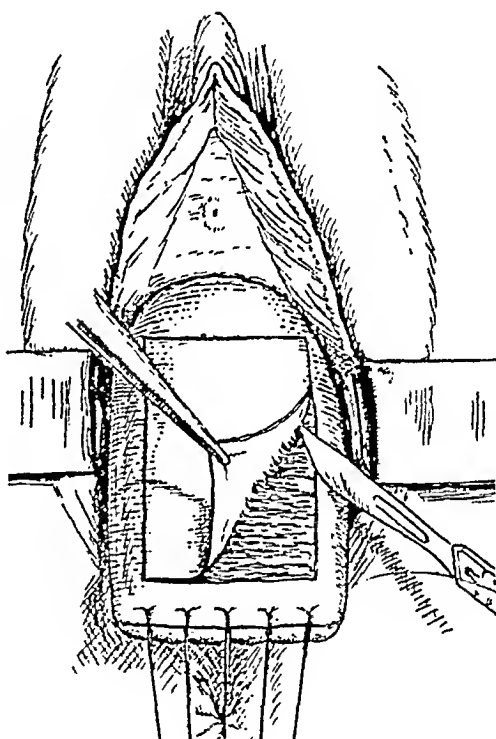


Fig. 2.

Fig. 1.—Subtotal Colpectomy. The cervix is dilated, the uterine cavity is curetted, the cervix, if eroded or lacerated, is amputated and reconstructed by means of chromic catgut sutures. When dealing with a prolapsed cervical stump, this is entirely removed and the edges of the vaginal wall are approximated with chromic catgut sutures. (LeFort)

Fig. 2.—Subtotal Colpectomy. The prolapsed cervical stump has been removed and the vaginal wall approximated by chromic catgut sutures. A rectangle of vaginal mucosa on the anterior vaginal wall has been outlined and is in process of being resected. (LeFort)

bladder or cystocele, the urethra or urethrocele, the rectum or rectocele, and the culdesac of Douglas or posterior vaginal enterocele. The term prolapse, in this paper, is used in its general sense.

While palliative measures such as pessaries and other mechanical measures may give relief in prolapse, surgery is the only curative method.

Surgical procedures are divided into two general classes: (1) the combined operation consisting of repair or amputation of the cervix, anterior and posterior colporrhaphy, and perineorrhaphy, followed by an abdominal operation as shortening of the uterosacral ligaments, uterine suspension or fixation, or supracervical hysterectomy with fixation of the stump, etc. (2) The vaginal operations, such as the interposition operation, vaginal hysterectomy with the interposition of the united broad ligaments (Mayo technic), and the high vaginal fixation of the uterus which Curtis<sup>1</sup> describes in his Textbook as the advancement operation, are three in common use although there are others. A proper repair of the pelvic

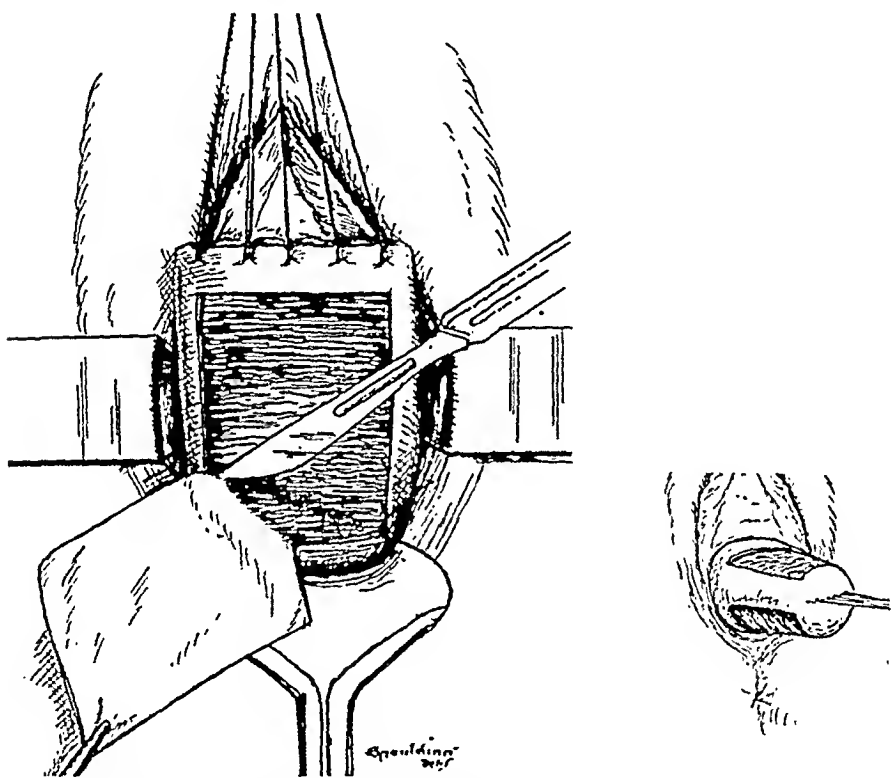


Fig. 3.—Subtotal Colpectomy. A rectangle of vaginal mucosa on the posterior vaginal wall has been outlined and is in process of being resected. The anterior and posterior rectangles should be of uniform dimensions. The insert shows the completed dissection. (LeFort)

floor is a complement to all the vaginal methods. George Gray Ward<sup>2</sup> has emphasized the fact that a hernia of the culdesac of Douglas should be attended to by resecting the culdesac and approximating the uterosacral ligaments while operating for a relaxed or lacerated perineum. The vaginal procedures which are relatively free from shock and which give excellent results are selected by the majority of pelvic surgeons, especially when operating on older women. They are also responsible for increasing the operability in this group of cases as they may be performed with safety when one would hesitate to do a laparotomy.

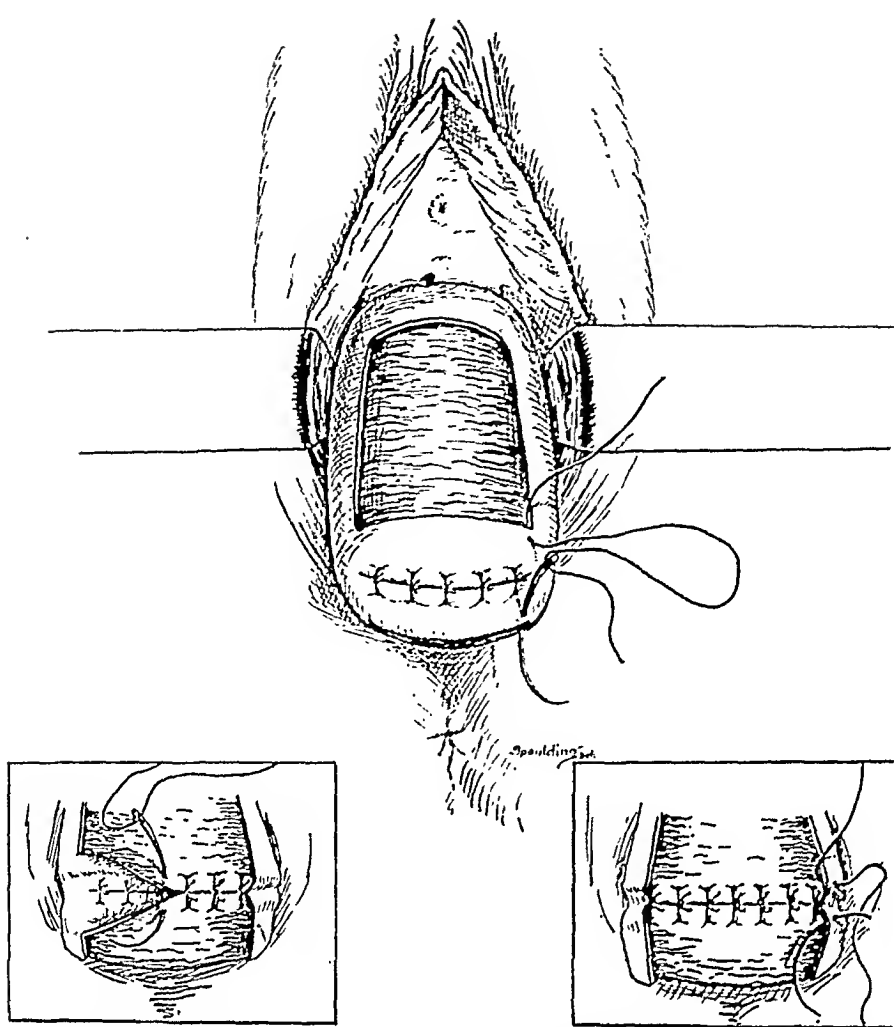


Fig. 4.—Subtotal Colpectomy. The inferior, then the lateral edges of the denuded areas are approximated by means of chromic catgut sutures. At the completion of this step of the operation, a superior and two lateral drainage canals, lined with vaginal mucosa, are formed. (LeFort)

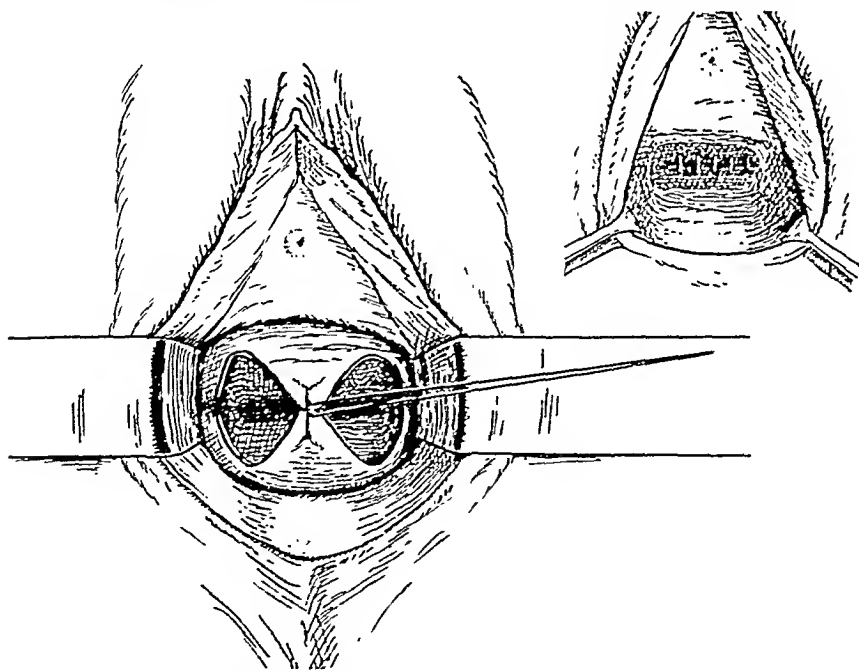


Fig. 5.—Subtotal Colpectomy. The superior edges of the denuded areas are now approximated with chromic catgut sutures. The prolapsed mass is now reduced. The insert shows this part of the operation completed. (LeFort)

While prolapse may be cured by the above mentioned methods, there is a group of women whose physical condition precludes the use of extended procedures and another group suffering from total inversion of

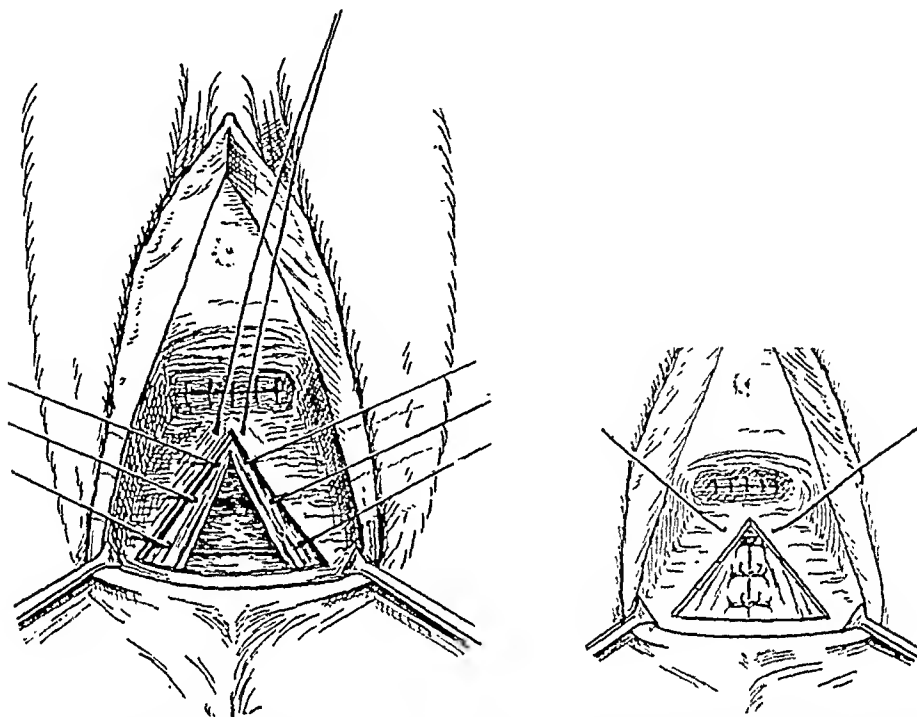


Fig. 6.—Subtotal Colpectomy. The perineum is denuded exposing the levator ani muscles and their covering fascia. The levators and their fascia are approximated by three chromic catgut sutures. The vaginal edges are next united by similar sutures. (LeFort)

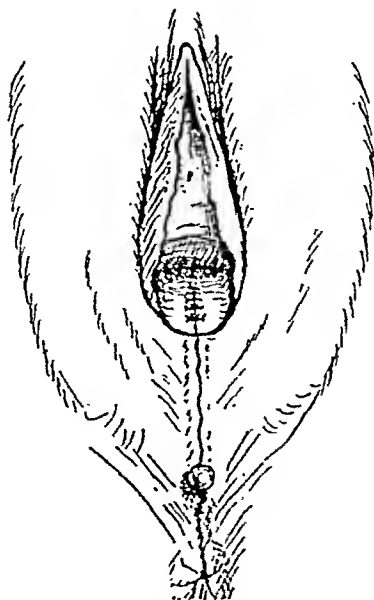


Fig. 7.—Subtotal Colpectomy. The external perineum is finished by a subcuticular stitch of fine chromic catgut, the end of which is held by a lead shot. The operation is completed. (LeFort)

the vagina following supracervical or total hysterectomy who are not easily cured by the ordinary methods. It is in this group of patients

that colpectomy, subtotal or total, plays its most important rôle. The operation is simple and may be performed with success even on poor surgical risks. Local infiltration anesthesia may be used to advantage if there is a contraindication to general or spinal anesthesia.

Léon LeFort<sup>3</sup> in 1877, described his operation, which is a subtotal colpectomy in which a rectangular area is denuded on the anterior and posterior walls of the prolapsed mass and the edges of these raw areas united by properly placed chromic catgut sutures. At the completion of the operation the cervix and corpus uteri are situated high above the newly constructed barrier. A superior canal below the cervix

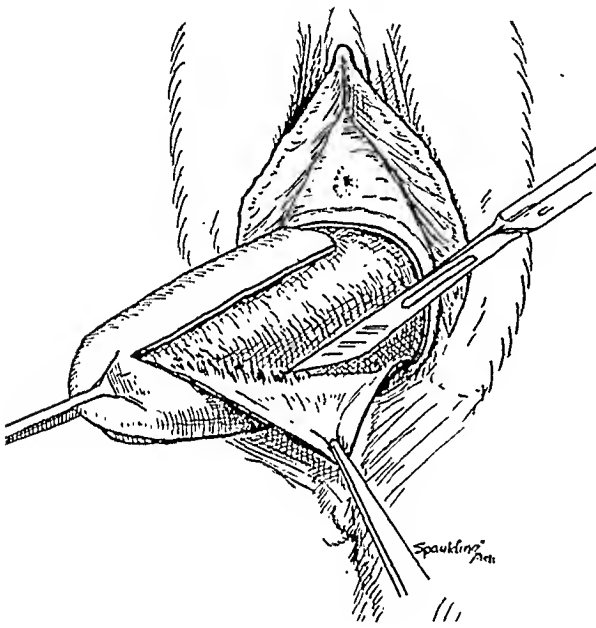


Fig. 8.

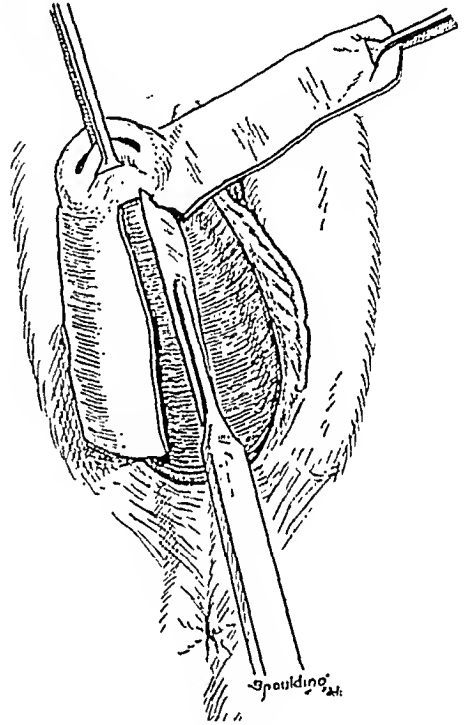


Fig. 9.

Fig. 8.—Total Colpectomy. Traction is made on the cervix and a circular incision is made in the vaginal wall about 2 cm. below the urinary meatus. An anterior and a posterior longitudinal incision is made in the median line, starting at the circular incision and ending a few centimeters from the cervix. The vaginal incisions must go through the entire thickness of the vaginal wall in order to find the line of cleavage between the bladder and the rectum and the vaginal wall. One side of the vagina is dissected free from its attachments. (Dujarier and Larget)

Fig. 9.—Total Colpectomy. One-half of the vagina has been dissected and is now resected from the cervix. The other half of the vagina is treated in a like manner. Care should be taken to excise small fragments of vaginal musosa which might remain adherent to the denuded surface. (Dujarier and Larget)

and two lateral canals are left for the purpose of drainage. This operation has been enlarged upon by making the anterior and posterior rectangles wider than called for in the original procedure, thus increasing the width of the supporting column but narrowing the lateral drainage canals. Amputation of the cervix, when it is the seat of laceration, irritation, or erosion, is a necessity, and repair of the perineum, by approximating the levator muscles and their investing fascia in the middle line, further adds to the support.

Total colpectomy was devised by Dujarier and Larget and well described by Hartmann.<sup>4, 5</sup> In this case a circular vaginal incision is made slightly below the level

of the urinary meatus and another above the level of the cervix, the vaginal wall is incised in the middle line, anteriorly and posteriorly, these incisions joining the lateral ones, the vaginal wall is then entirely removed in two halves, the cervix is amputated, and the cervical lips approximated by interrupted sutures of chromic catgut. Twelve strands of silkworm gut are tied in the central catgut stitch and form a drain from the uterine cavity when the operation is terminated. The bladder and rectum are united in superimposed layers by fine sutures of chromic catgut. Finally, the edges of the circular vaginal incision, below the urinary meatus, are united by interrupted sutures of No. 2 chromic catgut. The prolapsed mass is thus

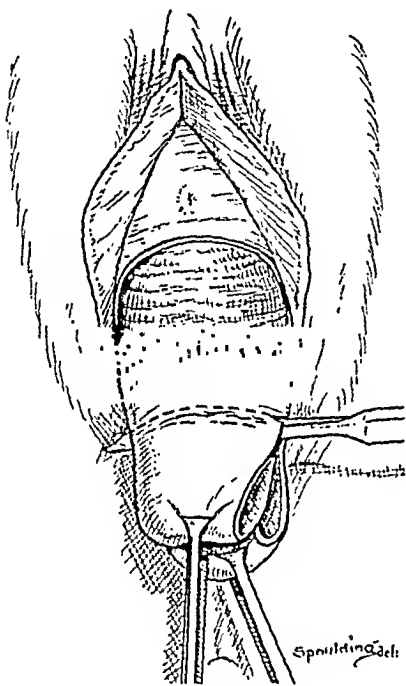


Fig. 10.

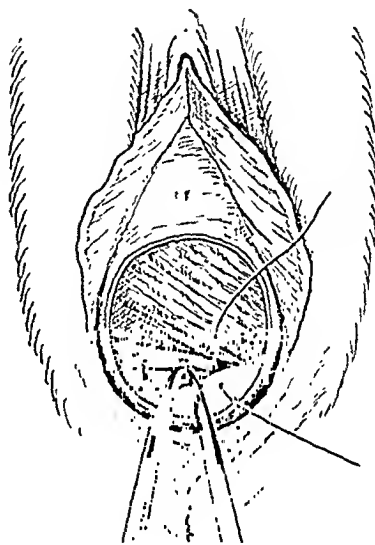


Fig. 11.

Fig. 10.—Total Colpectomy. The two halves of the vagina have been removed. The cylinder, making the prolapse, is entirely denuded up to the cervix. The uterovesical ligament is cut and the bladder is separated from the uterus. The cervix is next split with a knife and the anterior and posterior lips are amputated in the order mentioned. The cervical lips are united with three chromic catgut sutures. About twelve strands of silkworm gut are tied in the central stitch, over the cervical canal, and act as a drain. (Dujarier and Larget)

Fig. 11.—Total Colpectomy. The silkworm gut drain is shown. The bladder and rectum are united with sutures of fine chromic catgut, care being taken that the needle does not perforate these organs. Two or three planes of sutures are usually sufficient to reduce the prolapsed mass. (Dujarier and Larget)

reduced and the vagina completely closed around the silkworm-gut drain. The drain usually falls out on the tenth postoperative day. The perineum is repaired as after the subtotal colpectomy or LeFort operation. The majority of patients are treated by subtotal colpectomy while total colpectomy is reserved for extreme cases. In either instance, a diagnostic curettage should be performed to rule out endometrial carcinoma before resorting to the intervention.

Two objections to colpectomy have been expressed: (1) the inaccessibility of the uterus for treatment, should carcinoma develop at a later date; (2) the obliteration of the vaginal tube, precluding sexual relations. It is a recognized fact that carcinoma seldom develops in an

atrophied uterus and, since colpectomy is usually done on women whose uteri have undergone senile atrophy, the possibility of the development of carcinoma is very slight. The protection against carcinoma is increased by amputating the cervix, thus removing that part of the uterus on which malignant disease more frequently occurs. When this operation is performed on women who have had supracervical hysterectomies, removing the retained cervix as a preliminary step eliminates entirely the danger of carcinoma of the stump. The closure of the vagina in

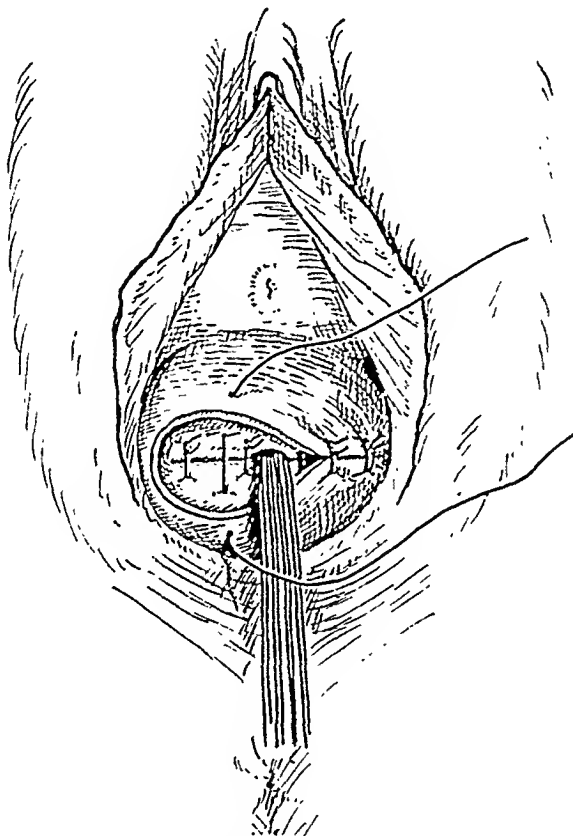


Fig. 12.—Total Colpectomy. The edges of the vaginal walls are approximated with sutures of ehromic catgut. The silkworm gut drain allows the escape of blood and serum and also allows the persistence of a small drainage canal, permitting the escape of uterine secretions, should any form. (Dujarier and Larget)

Although the original operation does not call for it, a perineorrhaphy may be added with considerable advantage.

old patients suffering from total prolapse of the uterms offers no serious objection, since the sexual life of these women is of no great importance. Except under very rare exeptions, colpectomy should not be employed in the younger group of women still sexually active.

The technic of subtotal colpectomy and of total colpectomy, for the sake of clearness, is described by means of drawings and accompanying legends.

I desire to present herewith my results in a series of twenty-five personal cases.

# STATISTICS

## COLPECTOMY

Subtotal colpectomy (LeFort). Enlarged	20
Total colpectomy (Dujarier and Larget)	5
	<hr/>
Total	25

## SUBTOTAL COLPECTOMY

LeFort operation 20 cases

### AGES

45 to 49 years	2
50 to 54 years	2
55 to 59 years	6
60 to 64 years	2
65 to 69 years	4
70 to 74 years	4 20 cases

The youngest patient was 47 and the oldest 72 years of age.

## INDICATIONS

Procidentia	7
Recurrent procidentia	3
Nulliparous procidentia	2
Inversion of vagina following abdominal supraecervical hysterectomy	4
Inversion of vagina following abdominal panhysterectomy	2
Inversion of vagina with atrophied uterus	2
Total	<hr/> 20 cases

## ADDITIONAL DIAGNOSES

Posterior vaginal hernia (large)	4
Calcified tumor of right ovary	1
Ulceration of vagina	1
Ulceration of cervix	4
Ankylosis of both knees	1
Total	<hr/> 11 cases

## OPERATION

LeFort operation (enlarged)	20
Amputation of cervix	5
Perineorrhaphy	19

In the case of one woman, sixty-six years of age, who had a nulliparous prolapse, the cervix was amputated, the LeFort operation was performed but the perineum was not repaired as it gave good support.



## ANESTHESIA

Local anesthesia	5
Spinal anesthesia	5
General anesthesia (ether)	10
Total	<u>20</u> cases

## RESULTS

Mortality	0
Recurrences	2
Satisfactory results	18
Total	<u>20</u> cases

## RECURRENCES

2 recurrences in 20 cases, or 10 per cent.

CASE 8.—A woman, sixty-five years of age, who had an enormous procidentia, an atrophied uterus, a large cystocele, a large rectocele, and a large hernia of the culdesae of Douglas, was operated upon on December 7, 1927. As a result of the marked atrophy and poor blood supply of the vaginal walls, low grade sepsis set in and the union of the flaps was poor. The cervix appeared at the vulva, after healing by second intention had taken place. On March 9, 1928, a laparotomy was performed. A calcified tumor of the right ovary, 7.5 by 7.5 cm. approximately, was removed, together with the right tube, and the uterus was fixed to the anterior abdominal wall by three linen sutures. At the time of the last examination, the uterus was held against the anterior abdominal wall, there was no prolapse of the uterus, bladder, rectum, or culdesae of Douglas and the patient was getting along comfortably.

CASE 18.—A woman, sixty-one years of age, had a total inversion of the vagina following an abdominal panhysterectomy. She was operated upon on June 1, 1931, the LeFort operation and a perineorrhaphy being performed. On June 8, the vagina had to be packed because of secondary hemorrhage. On June 15, secondary hemorrhage recurred and the vagina was packed again. Healing took place by second intention but the result was only fair.

## TOTAL COLPECTOMY

5 Cases

Ages—57, 59, 62, 64, and 64 years

## INDICATIONS

1. Procidentia, small atrophied uterus, marked ulceration of cervix, enormous posterior vaginal hernia.
2. Inversion of vagina following abdominal supracervical hysterectomy, severe erosion of the cervix.
3. Inversion of vagina following abdominal supracervical hysterectomy, five previous operations for prolapse.
4. Procidentia, deep ulceration of the cervix.
5. Inversion of vagina, large posterior vaginal hernia.

## OPERATION

Total colpectomy	5
Amputation of cervix	5
Perineorrhaphy	5

## ANESTHESIA

Local anesthesia	1
Spinal anesthesia	2
General anesthesia (ether)	2

## COMPLICATIONS

CASE 5.—A feeble woman, sixty-four years of age, had a recurrent procidentia following vaginal plastics and uterine suspension performed twenty-seven years previously; this was accompanied by total inversion of the vagina and a large posterior vaginal hernia. On March 17, 1930, a total colpectomy, amputation of the cervix and a perineorrhaphy were performed under spinal anesthesia. Healing took place satisfactorily and she was discharged with a good result. On Aug. 6, 1930, she had a purulent discharge escaping from the central drainage tract. Under spinal anesthesia a sound was introduced in the sinus and, at a depth of about 10 cm. an abscess was broken into with the escape of about 90 c.c. of thick green pus. The central canal was dilated and gently curetted; the material removed was examined histologically and reported as granulation tissue. The sinus was irrigated daily until clean, after which it readily healed. Examination several months after her discharge from the hospital showed a good result.

## RESULTS

Mortality	0
Recurrences	0
Satisfactory result	5

## CONCLUSIONS

1. Colpectomy as devised by Léon LeFort, in 1877, had been almost given up for years. More recently, the operation has been revived and somewhat modified in technic.

2. In old women colpectomy, subtotal (LeFort) or total (Dujarier and Larget), gives excellent results without subjecting the patient to undue operative risks.

3. Because of its benignancy and the simplicity of its performance, colpectomy permits increasing the operative incidence in these women.

4. Inversion of the vagina following supracervical or total hysterectomy may be easily cured by colpectomy.

5. Colpectomy may be performed under local infiltration or spinal anesthesia when general anesthesia is contraindicated.

6. A proper repair of the pelvic floor adds to the efficacy of the operation.

7. The end-results of twenty-five personal cases are reported.

## REFERENCES

- (1) *Curtis, A. H.*: A Textbook of Gynecology, Philadelphia, London, 1934, W. B. Saunders Co., pp. 239-252. (2) *Ward, G. G.*: J. A. M. A. 79: 709, 1922. (3) *LeFort, Léon*: Bull. gén. de thérap. 92: 337, 1877. (4) *Hartmann, Henri*: Gynéc. et Obstét. 11: 452, 1925. (5) *Dujarier and Larget*: J. de chir. 25: 283, 1925. (6) *Brocq, P., and Nora, G.*: Gynéc. et Obstét. 11: 338, 1925. (7) *Crousse, R.*: Bruxelles-méd. 14: 392, 1929. (8) *Bellas, J. E.*: Am. J. Surg. 25: 258, 1934. (9) *Rubovits, W., and Litt, S.*: AM. J. OBST. & GYNEC. 29: 222, 1935.

## ANALYSIS OF END-RESULTS OF LABOR IN PRIMIPARAS AFTER SPONTANEOUS VERSUS PROPHYLACTIC METHODS OF DELIVERY

ALBERT H. ALDRIDGE, B.S., M.D., F.A.C.S., AND PAUL WATSON, A.B.,  
M.D., NEW YORK, N. Y.

*(From the Obstetric Service of the Woman's Hospital)*

EVALUATION of end-results of obstetric practice by the usual standards, maternal and fetal mortality, and the incidence of pelvic infections which have caused elevation of temperature, fails to take into account many serious accidents and complications of labor and delivery.

It is a well recognized fact that mortality statistics, although positive in themselves easily obtained, present a very incomplete picture of the handling of groups of obstetric patients. Furthermore, conditions such as the toxemias of pregnancy, hemorrhage, surgical shock, or severe birth injuries may leave a patient with less margin of safety, and more permanent discomfort and disability, than most pelvic infections which are justly regarded with so much concern.

It is self-evident that our aim should be to develop and apply methods which will not only reduce the incidence of mortality in mothers and babies, but will also prevent accidents, complications, and birth injuries which may either immediately be dangerous or productive of physical handicaps in after life.

The Obstetrical Department at the Woman's Hospital was opened in 1917. From the beginning, members of the staff have delivered an increasing percentage of patients by methods which have since come to be known as prophylactic. The impression has been that by these methods the incidence of birth injuries and complications to both mothers and babies has been reduced. In view of all the discussion for and against such obstetric procedures, the time seemed opportune to make a comparative study of end-results of labor and delivery, especially in cases delivered by spontaneous and prophylactic methods.

Cases used in the study were 2,800 primiparas, delivered on our ward service during the years 1920 to 1925, inclusive, and from 1930 to 1934, inclusive. Patients delivered in the earlier years were selected for comparison with patients delivered more recently, because in those years a large percentage was allowed to deliver spontaneously. In the later years, 1930 through 1934, a higher percentage of patients was delivered by prophylactic methods. Only primiparas were studied, for the obvious

reason that whatever permanent birth injuries were found, following delivery, could be directly attributed to the delivery. This gave an opportunity to make a more or less exact comparison of end-results after the various methods.

It is of interest that over 95 per cent of the patients in the series were delivered by hospital internes. The remaining 5 per cent were delivered by an attending surgeon, or an interne under supervision of an attending surgeon. In other words, the study is of the end-results of a system of obstetric practice in a hospital service equipped for gynecology and obstetrics. The actual work upon which the results are based has been almost entirely done by 88 hospital internes being trained in gynecology and obstetrics.

Table I shows age distribution, in percentages, of the cases studied.

TABLE I. AGE DISTRIBUTION OF 2,800 PRIMIPARAS

AGE	PER CENT
Up to 20	10
20 to 25	42
25 to 30	31
30 to 35	12
35 to 40	4
Over 40	1

As cases were studied, they divided themselves naturally into six distinct groups according to the methods of delivery employed:

1. Spontaneous
2. Spontaneous after perineal incision
3. Perineal incision and elective low forceps
4. Operative
5. Operative after perineal incision
6. Patients delivered by the abdominal route

Patients delivered by "elective low forceps" are those who would have delivered spontaneously if allowed to do so. All other forceps deliveries referred to later as "indicated forceps operations" were necessary for the protection of the mother, of the baby, or of both.

Midline perineal incision is now used almost routinely in the delivery of primiparas because: (1) It is easier to repair and is more likely to heal by primary union; (2) it avoids injury to the levator muscle.

The disadvantage of the midline incision is that if extension occurs, the anal sphincter and rectal mucosa may be injured. In this series, extension partially through the sphincter occurred in 4.4 per cent and completely through the sphincter in 3.2 per cent. No case in the series had fecal incontinence as a result of loss of sphincter control. One patient had a small rectovaginal fistula.

The technic used in the closure of perineal wounds has been exactly like that described by Goff for secondary repair of lacerations of the pelvic floor and posterior vaginal wall. It will be noted that the perineal body is repaired by catgut sutures, which are entirely subcutaneous. We believe that through and through nonabsorbable sutures, frequently used in the primary repair of perineal incisions or lacerations, predispose to infection and cause unnecessary discomfort.

It is self-evident that the benefits, to be derived from elective low forceps, may be lost and unnecessary or irreparable damage may be done, unless the procedure is used under satisfactory conditions, and by an operator with sufficient ability and training to: (1) Make an exact

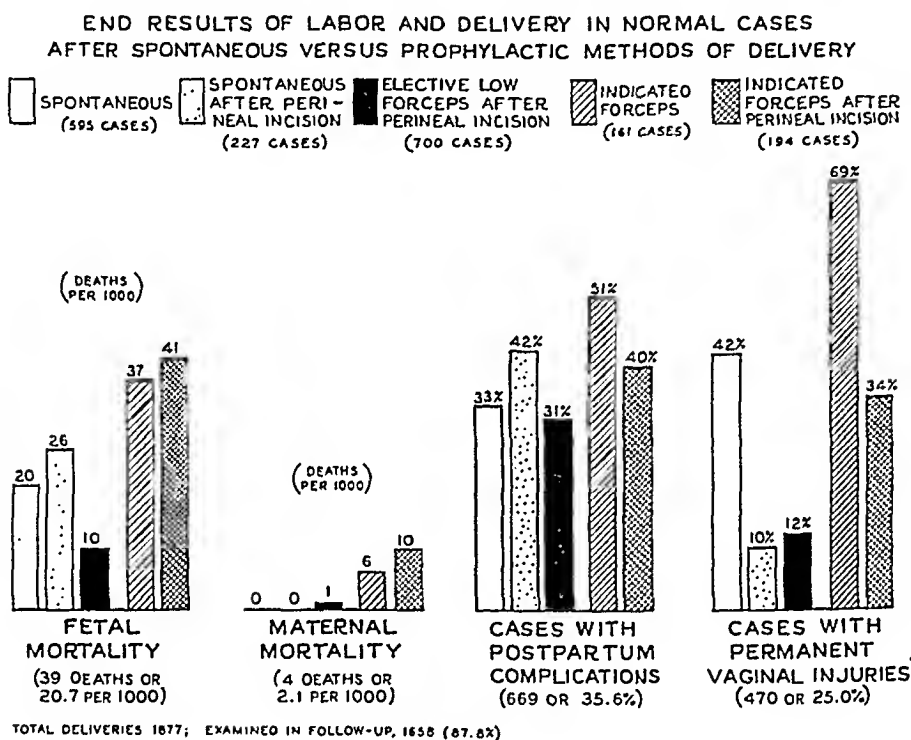


Chart 1.

diagnosis of the presentation, position and level of the presenting part. (2) Apply forceps correctly, and deliver the baby with a minimum of trauma.

We wish to emphasize the fact that elective forceps operations should not be done until, as Dr. Lee advises, "the head has come well down on to the pelvic floor, in complete anterior rotation, and has begun to part the levator ani pillars."

Physical findings noted in the follow-up were used as a basis for comparison of end-results in patients delivered by the various methods. Approximately 88 per cent of patients delivered were examined, at least once, six weeks after delivery by one or more attending surgeons who were specializing in gynecology as well as obstetrics.

All cases showing laceration or definite relaxation of the pelvic floor or vaginal walls were considered abnormal.

A summary of the end-results of labor and delivery in 1,877 normal cases is shown in Chart 1. This group included only women with normal pelves who went into labor spontaneously at term, with a vertex presentation, an anterior position, or a posterior position with spontaneous rotation.

We note that:

1. The incidence of fetal mortality and postpartum complications, in patients delivered by elective low forceps after perineal incision, was lower than in spontaneous deliveries.

2. Perineal incision, whenever used, strikingly reduced the incidence of cases, with permanent birth injuries.

3. There was no maternal death in patients delivered spontaneously. One maternal death after elective low forceps was the result of sepsis caused by retained placental tissue.

The relatively high incidence of fetal and maternal deaths, postpartum complications, and patients with birth injuries which occurred in the 194 patients delivered by indicated forceps after perineal incision as compared with the 161 patients delivered by forceps alone, can be explained by two facts as follows: (1) In the group delivered by forceps alone, 65 per cent had prolonged labors as compared with 87 per cent in the other group. (2) End-results were undoubtedly influenced by the type of forceps operation required to complete the delivery as noted in Table II. From this table it will be noted that nearly twice as many patients were delivered by midforceps after perineal incision as in the group delivered by forceps alone.

TABLE II. NORMAL CASES. SUMMARY, IN PERCENTAGE, OF THE VARIOUS TYPES OF OPERATION REQUIRED IN PATIENTS DELIVERED BY INDICATED FORCEPS

TYPE OF FORCEPS OPERATION	METHOD OF DELIVERY	
	FORCEPS NO. OF PATIENTS 161	FORCEPS AFTER PERINEAL INCISION NO. OF PATIENTS 194
Low	77	60
Mid	22	39
High	1	1

The relatively low incidence of fetal mortality, associated with delivery by prophylactic low forceps, is significant. It is fair to assume that any method of delivery which is attended by a low incidence of fetal mortality, is also attended by a correspondingly low incidence of babies with birth injuries which are not fatal. Unfortunately, the babies delivered in this series could not be followed for a sufficient period of time to confirm this assumption.

In Chart 2 is demonstrated to what extent and how consistently perineal incision is a prophylactic measure in preventing permanent vaginal birth injuries in various types of cases.

Normal cases, with prolonged labor, were selected by the same standards as those in Chart 1, but were studied separately to determine the effect of prolonged labor in the causation of vaginal injuries.

In the prolonged group were included all normal cases in which labor had not terminated within twenty-four hours, or in which the second stage had exceeded two hours in duration. From this it is evident that the pressure of prolonged labor may in itself be an important factor in the causation of permanent vaginal birth injuries.

It also shows the end-results following delivery at term of 227 women with contracted pelves causing excessive pressure during labor and a

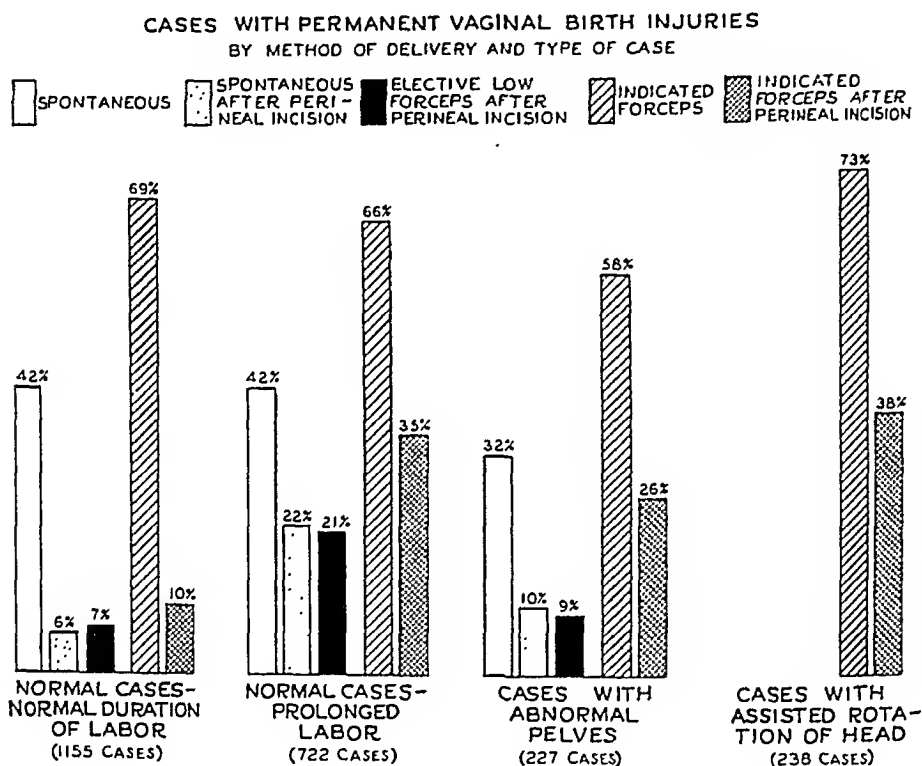


Chart 2.

definite increase in vaginal injuries as compared to end-results in cases with normal pelves.

Although statistics are not recorded on this chart, the relationship of the size of the baby to the incidence of birth injuries was studied and showed convincing evidence that excessive pressure from large babies was another definite factor in the causation of vaginal birth injuries.

The incidence of cervical lacerations varied from 34 to 46 per cent in the various types of cases and the uterus was found to be retroverted in from 16 to 25 per cent of the cases in the various groups studied.

Of the 238 patients with persistent occiput posterior position, 6 were delivered as occiput posterior, and in the remaining 232 patients, rotation was accomplished as follows: manual 55, Scanzoni 155, and Kielland 22. Following rotation 5 babies were delivered spontaneously. Of

CASES WITH PERMANENT INJURIES TO PELVIC FLOOR  
BY METHOD OF DELIVERY AND TYPE OF CASE

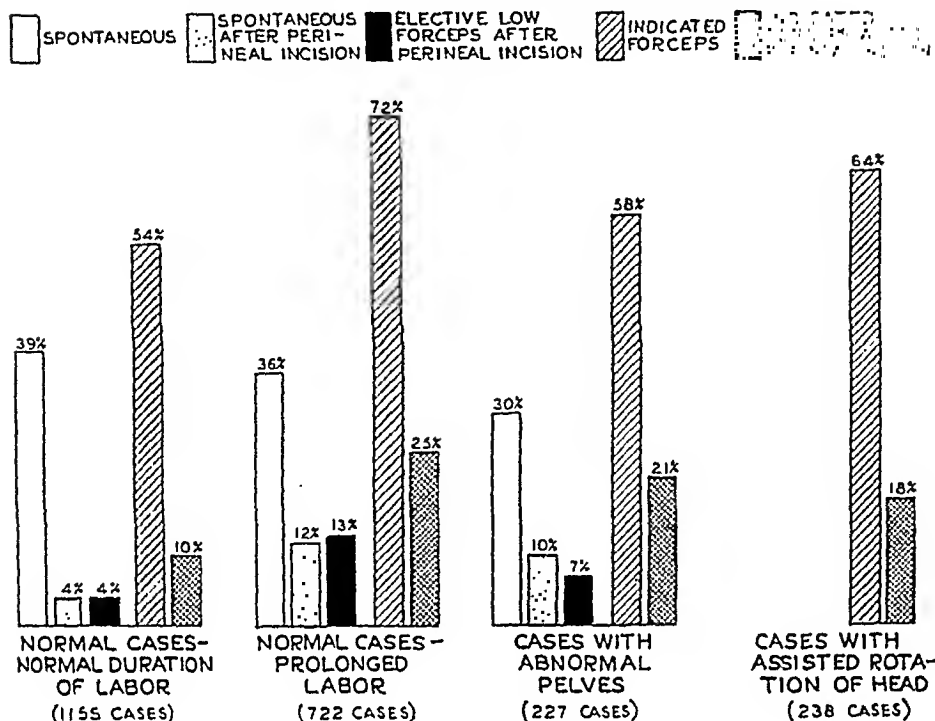


Chart 3.

CASES WITH PERMANENT INJURIES TO ANTERIOR VAGINAL WALL  
BY METHOD OF DELIVERY AND TYPE OF CASE

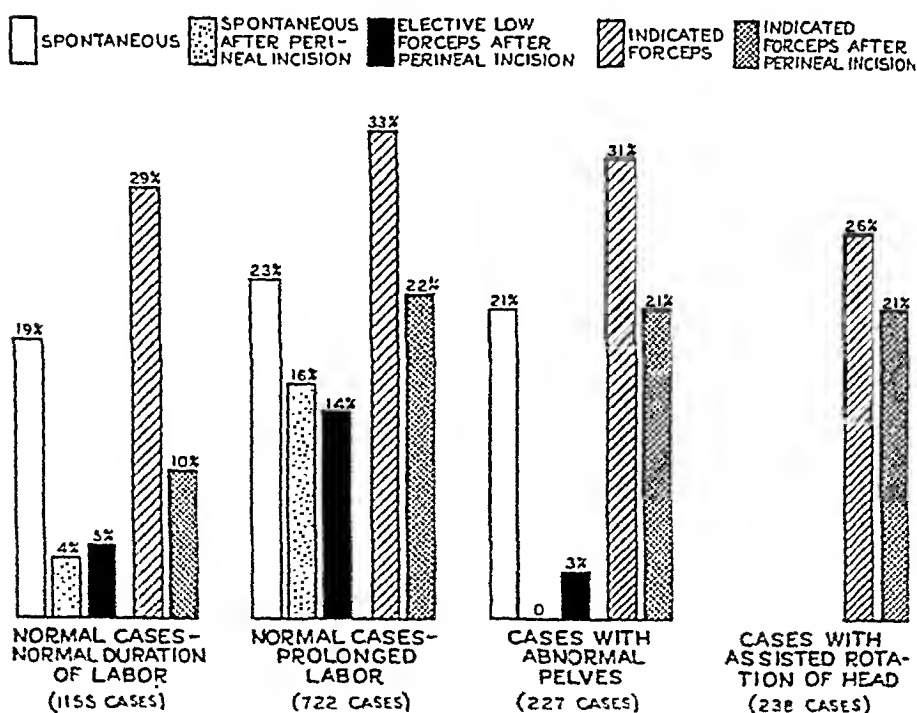


Chart 4.



the 233 delivered by forceps, operations were classed as follows: low 60, mid 157, and high 16. The number of patients delivered as occiput posterior was too small to be recorded.

The graphs shown in Chart 3 demonstrate in a rather striking way to what extent prophylactic methods of delivery prevent permanent injuries to the pelvic floor in various types of cases.

From Charts 4 and 5 it is evident that perineal incision greatly reduces the incidence of permanent injuries to the anterior and posterior vaginal walls. These graphs indicate that the procedure is as effective in preventing injuries to the anterior wall as it is to the posterior wall. A comparison of the two indicates that in prolonged labor the percentage

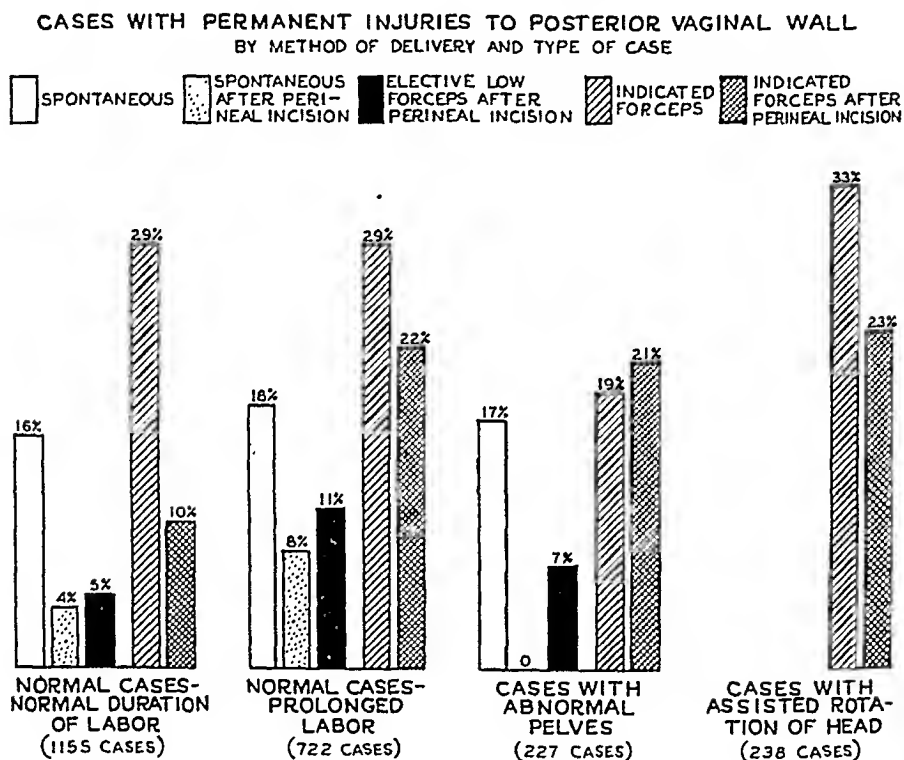


Chart 5.

of patients with injuries to the anterior wall increases more than does that of injuries to the posterior wall.

The incidence of vaginal injuries in breech deliveries is shown in Chart 6 and indicates that perineal incision is a prophylactic measure in every type of delivery.

In this group are included 94 patients who presented as breech and 28 patients who were delivered by version and extraction.

A comparison of physical findings, during the early days when a high percentage of patients was allowed to deliver spontaneously, with those of later days when a high percentage was delivered by prophylactic methods, is not an entirely fair or accurate one, for in the early days certain injuries to the cervix and pelvic floor and permanent relaxations of the

vaginal walls were considered inevitable and therefore within normal limits. We now consider injuries to the pelvic floor and vaginal walls to be preventable in such a high percentage of cases, that they are recorded as definite birth injuries, rather than physiologic changes incidental to delivery.

It is now our custom to discharge from our follow-up six weeks after delivery, patients free from birth injuries. Large numbers of patients kept under observation for long periods of time have convinced us that the result at six weeks so rarely changes, that it can be considered a final one.

CASES WITH PERMANENT VAGINAL BIRTH INJURIES - BREECH DELIVERIES  
BY METHOD OF DELIVERY

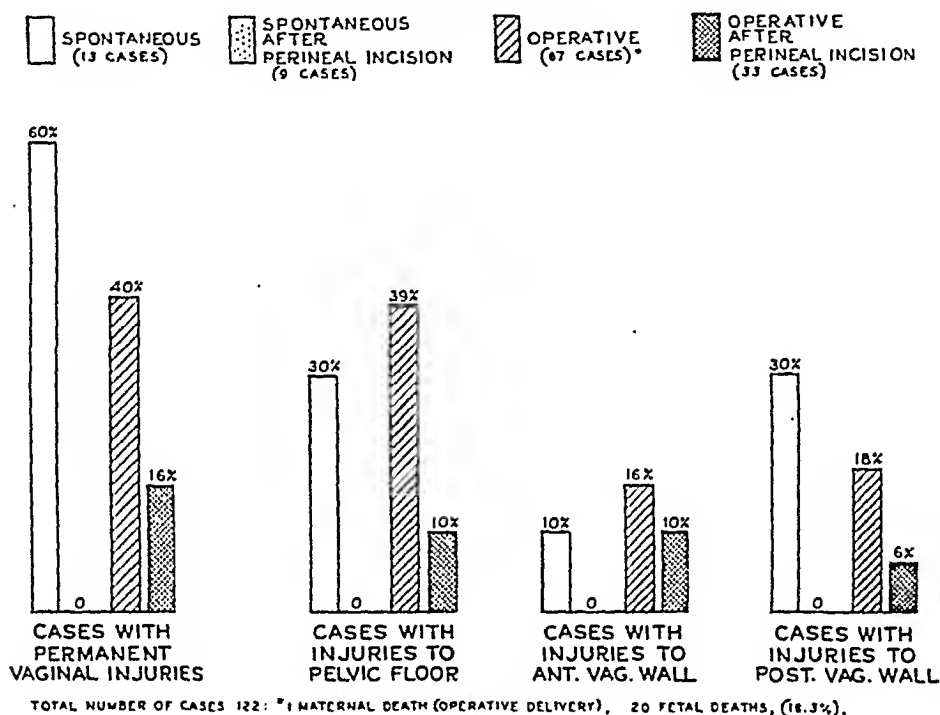


Chart 6.

Patients with postpartum cervical injuries and erosions are treated with electrocoagulation, and such patients are kept under observation until healing is complete. Retroversion is treated with posture and in some patients with pessaries. We find that if the vaginal walls are not abnormally relaxed by delivery, pessaries large enough to give proper support are difficult to insert. Consequently, we have used fewer pessaries since more patients have been delivered by elective methods.

Table III is a summary of cases delivered by the abdominal route and results obtained.

Of the 2,800 primiparas selected for this study, 82 or 2.9 per cent were delivered by the abdominal route. In the past few years, since the advantages and relative safety of low flap and extraperitoneal (Latzko) cesarean section have been established, the classical operation is rarely

done, and the incidence of delivery by the abdominal route has increased to a point considerably higher than that shown in this series.

In the interest of both mothers and babies, we now consider cesarean section the method of choice for the delivery of women with obstructed labor from contracted pelvis, or cervical dystocia, and for those women in whom delivery is complicated by placenta previa. It is also used in selected cases for the delivery of women who are the victims of arrested tuberculosis, cardiac disease, or toxemia of pregnancy.

TABLE III. DELIVERIES BY THE ABDOMINAL ROUTE

INDICATION	NUMBER OF CASES	TYPE OF CESAREAN			FETAL MORTALITY
		CLAS-SICAL	LOW FLAP	LATZKO	
Contracted pelvis	26	14	11	1	—
Toxemia of pregnancy	15	2	13	—	—
Cervical dystocia	15	—	11	4	—
Obstructed labor	5	1	4	—	—
Disproportion	5	—	4	1	—
Tuberculosis	5	1	4	—	—
Placenta previa	4	1	3	—	1*
Premature separation of placenta	3	—	3	—	1†
Elderly primiparas	2	1	1	—	—
Cardiac disease	1	—	1	—	—
Full-term abdominal pregnancy (hysterectomy)	1	—	—	—	—
Total	82	20	55	6	2

\*Baby dead at term before operation.

†Baby macerated at twenty-eight weeks' gestation. No maternal mortality. Operations: Elective, 28; after trial labor, 54.

Intelligent use of cesarean section demands careful study of patients in the antepartum period and expert handling and observation in the early hours of labor. With a proper understanding of acceptable indications and a careful study of individual patients, we feel that of all sections done, the incidence of elective operations could be increased and that on the whole, the decision to deliver a patient by the abdominal route, after trial labor, might frequently and advantageously be made somewhat earlier.

Furthermore, we are now convinced that in the hands of men well trained in gynecology and obstetrics, cesarean section may be used as a method of delivery, in certain borderline cases, with sufficient safety to allow the welfare of the child to be considered.

Table IV presents a summary of all postpartum complications. The incidence of sapremia is high owing to the fact that the diagnosis was not based entirely on an arbitrary level of temperature. We believe that a slight but continued rise of temperature above normal is often more significant than fever to a level sufficient to be classed as "infectious morbidity" by most prevailing standards.

We believe that postpartum morbidity should mean more than postpartum infection.

A recently published study of postpartum complications at the Woman's Hospital showed that patients may have significant complications without any elevation of temperature. Again, we wish to emphasize the need for a logical uniform standard for the determination of puerperal morbidity. Such a standard should be based on a consideration of all symptoms and physical findings rather than on a single symptom, such as fever.

TABLE IV. SUMMARY OF POSTPARTUM COMPLICATIONS FOLLOWING VAGINAL DELIVERIES

TYPE OF COMPLICATION	NUMBER OF CASES
Sapremia	565
Faulty wound union, pelvic floor	210
Mastitis, nonsuppurative	110
Urinary tract infections	54
Upper respiratory infections	48
Hemorrhage, 1°	41
Shock	33
Mastitis, suppurative	18
Hemorrhage, 2°	16
Fever, cause undetermined	12
Bronchitis	11
Pelvic infection	10
Thrombophlebitis	6
Pneumonia	3
Hemorrhage, 3°	3
Miscellaneous	27

Table V shows the incidence of fetal mortality and causes of death in premature and mature babies. There was a total of 2,824 (mature 2,617, premature 207) babies born. Of these babies, 150 (mature 94, premature 56) were stillborn or died within the first two weeks of life. In estimating fetal mortality, Stander has recommended that all babies weighing less than 1,500 gm. and that are less than 35 cm. in length be excluded. By this standard the total number of babies born would be 2,796 and the total number of fetal deaths would be 122, making the rate for fetal mortality 4.3 per cent or 43 deaths per 1,000.

TABLE V. FETAL MORTALITY

CAUSE OF DEATH	NO. OF DEATHS
Birth trauma	54
Cord pressure	14
Toxemia of pregnancy	11
Malformation	7
Premature separation of placenta	6
Infections	6
Atelectasis	5
Syphilis	2
Prematurity	1
Cause undetermined	16
Total	122
Total number of infants	2,796
Total number of fetal deaths	122
Percentage of fetal deaths	4.3

Table VI is a summary of all maternal deaths in the series.

Two deaths occurred in patients who became septic following delivery. The first was in a woman who had had a severe hemorrhage from placenta previa before admission. Following vaginal delivery of a baby presenting as a breech she became septic and died suddenly of what was thought to be a pulmonary embolism on the twenty-fourth postpartum day. The other septic death occurred in a woman in whom, at time of delivery, a succenturiate placental lobe was accidentally left in the uterus. This was removed on the thirteenth postpartum day on account of hemorrhage. The patient developed a nonhemolytic streptococci bacteremia and died on the thirty-sixth postpartum day.

Failure in recent years to reduce the incidence of maternal mortality continues to be a matter of great concern to obstetricians. In an accounting of the end-results of obstetric practice, perhaps attention has been too often focused on maternal and fetal mortality. Prevention of the serious complications, accidents, and birth injuries during labor and delivery, seems the logical means for reducing mortality. Again we are faced with the importance of antepartum care and the necessity for as careful preparation of the patient for delivery as would be demanded for any major surgical operation. The delivery should then be conducted in accordance with established surgical principles for the prevention of trauma, hemorrhage, surgical shock, and infection.

TABLE VI. MATERNAL DEATHS IN PRIMIPARAS

AGE	ANTEPARTUM OBSERVATION	COMPLICATION OF PREGNANCY	GESTA- TION (WEEKS)	CAUSE OF DEATH	POSTPARTUM COMPLICATION
33	None	Placenta previa	37	Pulmonary embolism*	Secondary anemia
38	None	None	40	Pulmonary embolism	None, afebrile
31	Satisfactory	None	40	Pulmonary embolism	Furunculosis
31	Satisfactory	Cardiac disease	40	Lobar pneumonia	Lobar pneumonia
29	Satisfactory	Toxemia	40	Bacteremia*	Retained placental tissue (removed 13th p.p. day)
37	None	Chronic nephritis	28	Uremia	Uremia
37	None	Chronic nephritis	24	Uremia (died undelivered)	—

Total number of deliveries—vaginal 2,718; abdominal 82; total 2,800.

Total number of deaths—7 (0.25 per cent) or 2.5 deaths per 1,000 births.

\*Deaths from sepsis—2 (0.071 per cent) or 0.71 deaths per 1,000 births.

#### CONCLUSIONS

1. The incidence of birth injuries to mothers and babies, and postpartum complications, were in direct proportion to the incidence of factors, such as prolonged labor, abnormal pelvis, faulty presentation, and large babies, which resulted in the application of increased pressure to the maternal soft parts and to the fetus during labor and delivery.

2. Elective low forceps after perineal incision can justly be regarded as a prophylactic procedure in patients who would deliver spontaneously if allowed to do so.

3. Perineal incision when used in conjunction with any type of vaginal operative delivery consistently reduced the incidence of birth injuries and postpartum complications.

4. Prophylactic methods of delivery should be used by men trained both in obstetrics and gynecology in hospitals properly equipped to give obstetric care.

5. Ideally, all women should have the protection of delivery in hospitals under supervision of men trained in gynecology and obstetrics.

#### REFERENCES

Ward, Goff, and Aldridge: Bull. Am. Coll. Surg. 19: 9, 1935. Goff: Surg. Gynec. Obst. 46: 855, 1928.

33 EAST SIXTY-EIGHTH STREET

---

## CLINICAL AND BACTERIOLOGIC OBSERVATIONS IN TRICHOMONAS VAGINITIS

EDWARD ALLEN, M.D., LLOYD B. JENSEN, PH.D., AND I. H. WOOD,  
CHICAGO, ILL.

(From Rush Medical College and Presbyterian Hospital)

DEFINITE proof is lacking as to which one of the many organisms found in the vaginal secretions of *Trichomonas vaginitis* is responsible for this condition.<sup>1-5</sup> The mode of primary infection is also still in need of explanation. The numerous and varied treatments which have been advised from time to time suggest that none of them is specific.<sup>6-10</sup> We have attempted in this study to correlate some of our clinical observations with bacteriologic data which we hope will be of interest in these problems.

*Symptoms.*—It has been shown repeatedly that *trichomonas* may be present in the vaginal secretion for long periods of time without producing symptoms. It would seem, therefore, that such individuals must have either developed an immunity to the infection or that there is lacking in these patients some additional element which would cause symptoms if present. It has been suggested by various investigators that this additional factor is most probably a streptococcus.<sup>2, 3</sup> Considerable evidence has already been produced which indicates that symbiotic union of a streptococcus and *Trichomonas vaginalis* is necessary for the production of symptoms.

When symptoms do occur they are usually characterized by an acute onset, often following conditions which result in lowered resistance. These low points in resistance may coincide with the menstrual period, respiratory infections, extreme fatigue, pregnancy, disturbances of the gastrointestinal tract, or sexual intercourse.

It has not been our experience that patients afflicted with *Trichomonas vaginitis* always present the clinical picture as it is usually described. The usual symptoms of vulvar itching and burning caused by the irritating vaginal discharge are frequently less severe than the urinary disturbances. Frequency of urination, dysuria, nocturia, and even incontinence are often so pronounced that the vaginal source of the disease may readily be overlooked. Our mistakes of diagnosis in this regard have been most frequent when the vaginal discharge was not profuse or when it retained its thick, mucoid or normal cheesy character. Several of our patients had been or were subjected to cystoscopy and pyelography before *Trichomonas vaginitis* was suspected.

During the course of the disease about one-fourth of our patients developed increased bleeding. This menorrhagia was often transitory and occasionally was associated with metrorrhagia. We do not believe that this increased blood loss can be ascribed alone to the unusual congestion in the pelvis. We are inclined to think that pelvic cellulitis secondary to *Trichomonas vaginitis* is a more common occurrence than is generally supposed. It is not unreasonable to suggest that these associated virulent streptococci may ascend the genital tract of women almost as readily as the gonococcus. Five of our patients had been examined vaginally before the onset of the menorrhagia and their pelvis found to be normal. Following the appearance of increased blood loss, examination revealed palpable tender adnexal swellings. This inflammatory reaction was severe enough to cause an elevation of temperature, and in three of these patients a leucocytosis of 12,400, 17,600 and 20,200 developed. Repeated examinations failed to reveal the gonococcus. Further confirmatory evidence of the invasive tendencies of these streptococci was obtained by culturing material taken from two Bartholinian abscesses. In both instances we were able to recover the same type of streptococcus as was found in cultures of the vaginal secretion. In an additional instance of acute Bartholinitis, however, associated with *Trichomonas vaginitis*, we were unable to obtain any growth of bacteria.<sup>8</sup>

The clinical picture of one of these patients was to us particularly interesting. For a period of about three years there had been present an increased discharge from the vagina. On several occasions during this time, usually following the menstrual period, an acute exacerbation of the vaginitis had occurred. In the course of the last acute attack the right Bartholin gland had become tender and swollen to the size of a large English walnut. At the same time a

monarticular arthritis, involving the left wrist, developed. The complement fixation test was negative and repeated slide examinations of the vaginal secretions revealed *Trichomonas vaginalis* but no gonococci. Drainage of the Bartholinian swelling followed by treatment of the vaginitis led to a slow but constant improvement in the pain and swelling of the wrist joint. Cataphoretic studies of the streptococci obtained from the Bartholin gland indicated that they were of the arthrotropic variety.

A rather large percentage of these women have exhibited arthritic and neuritic symptoms in other regions of the body. We shall attempt to indicate later in the discussion of the bacteriology that these focal infection syndromes may be due to associated bacteria of the streptococcus group. This evidence is further supported by the fact that some of these patients have been relieved of the joint and muscular symptoms by appropriate local or general treatment of the vaginitis.

We have tried most of the accepted methods of treatment with about the same average degree of success. Roughly, about 80 per cent of all of our patients have responded favorably and permanently to these various therapeutic measures. The remaining 20 per cent have had variable recurrent periods of infestation, some of them extending over a period of years. It is with this latter group that we have been particularly concerned and studies have been made along the following lines.

Bacteriologic studies have been made of the streptococci found in the vagina of patients suffering with *Trichomonas vaginitis*. At the same time similar cultures were taken from the nasopharynx. These cultures have been compared with cultures taken in the same manner from the vagina and nasopharynx of normal women.

We have compared the cultures obtained from patients responding readily to treatment with those in whom recurrences had occurred. Whenever possible we have searched for trichomonas in the prostatic secretion of the husbands of these women. In each case the culture of streptococcus obtained from the prostatic secretion has been compared with that isolated from the vaginal secretion of the wife. Attempts are being made to alleviate the condition by increasing the local and general resistance of these individuals.

All of these cultures were grown in tall columns of dextrose brain broth and on blood agar plates. The cultures were incubated for eighteen hours at 37° C. When colonies had been identified they were prepared for study in the cataphoretic cell. The apparatus used was a modified Northrop-Kunitz-Mudd assembly.

Many investigators<sup>11-13</sup> have demonstrated that bacteria carry electrical surface charges. When these bacteria are suspended in distilled water and an electrical current is passed through the cataphoretic cell, the organisms move toward the anode. On reversal of the current, move-



ment occurs toward the changed position of the anode. The velocity of this migration seems to indicate specificity and, therefore, helps to identify the organism.

Graphs have been prepared to represent the curves of the electrical potential. These graphs indicate that the streptococci isolated from the vagina of all patients afflicted with *Trichomonas vaginitis* fall in the same general area of electrical charge. By this method no difference in the electrical potential of the bacteria isolated from those patients responding readily to treatment and those exhibiting the recurrent and resistant infections could be determined. To us this fact seems to indicate that the difference between the transitory and resistant infection is more probably one of lowered resistance or reinfection of the host. These strains of streptococci were of the green-producing type. Especially in those patients complaining of joint and muscular symptoms cataphoretic examination of the cultures identified them as belonging to the group of arthrotropic or neurotropic streptococci.<sup>11</sup>

Streptococci cultured from a few normal vaginal secretions did not have the same electrical potential grouping as those from the vagina of affected cases. The cultures obtained from the nasopharynx of all patients have a distinctly different electrical potential grouping than those grown from normal or infected vaginal secretions. However, in one patient a strain was recovered from the substance of a tonsil after its removal which corresponded potentially with the strain isolated from the discharge caused by her *Trichomonas vaginitis*. Similar results were obtained in another patient where the material was secured from an infected tooth and compared with the bacteria from the infected vaginal secretion.<sup>14</sup>

The bacteria grown from the tooth and tonsillar tissue were injected into the blood stream of a rabbit. A suggestive localization in the cervix was noted. We have not been able, however, to infect the vagina of the rabbit with *trichomonas* either in its normal state or following intravenous inoculation with the specific strain of streptococci obtained from the infected human vagina.<sup>15-19</sup> We hope to investigate this possibility more thoroughly.

The most evident and logical source of reinfection should, of course, be sexual intercourse. Recently Dr. Norris J. Heckel has been co-operating with us in the prostatic examination of the husbands of patients having *Trichomonas vaginitis*. We have recovered *trichomonas* from the prostatic secretion in six of the husbands and in seven others have found evidence of a chronic prostatitis. The prostatic fluid has been cultured at the same time cultures were taken from the vagina of the wife. Streptococci of the same electrical potential have been ob-

tained in the nonspecific prostatitis without the trichomonas as in the secretion containing the flagellates. The graphs of the electrical potentials of the organisms from the prostatic secretions reveal that they are organisms similar to those found in the vagina. This finding has occurred with such regularity and under such suggestive conditions that we feel that both *Trichomonas prostatitis* and *Trichomonas vaginitis* may well be added to the list of venereal diseases.<sup>20-23</sup> Only three husbands in whom we were able to culture the prostatic secretion failed to reveal either the trichomonas or streptococci. The trichomonas disappear rapidly from the prostate with massage or by the application of heat. The streptococcal residue, however, is more resistant to treatment. Dr. Heekel has recently reported<sup>24</sup> some very encouraging results in the treatment of the more acute forms of streptococcal prostatitis, and he expects to extend his work to include these chronic forms. Constant transfer of these streptococci from host to host may very well increase the virulence of the organism. Constant transfer of these virulent organisms may institute the initial vaginitis and the trichomonas may well be the secondary invaders.

An instructive case history may best illustrate the points under discussion. This patient had been treated for a period of several months during which time there were three recurrences. Following one of these periods of treatment the patient left for a six months' vacation. During her absence she was entirely free from symptoms. Seven days after her return she came to the office complaining of an acute return of the typical symptoms. Five days later the husband appeared complaining of dysuria and a slight urethral discharge. The prostatic and vaginal fluids contained swarms of trichomonas and on culture many streptococci of the same electrical potential were found.

Resistance of the host is always the most important factor in combating infection. The relatively good results of so many types of different treatments which have been suggested for *Trichomonas vaginitis* leave one with the impression that their general efficacy depends upon raising the local resistance of the vagina rather than the bactericidal properties of therapeutic agents employed.

We have attempted to raise the general as well as local resistance. Rest, both physical and sexual, has been suggested. Adequate vitamin intake has been maintained. Prompt treatment of respiratory and gastrointestinal difficulties has been instituted.

Following the suggestive results reported in arthritis, neuritis, and gonorrhea by the use of vaccines and filtrates,<sup>21-27</sup> we have begun to inject intracutaneously into these patients preparations obtained from their individual growths of bacteria. As yet only suggestive results have been obtained. We expect to report them more fully at a later date.

## REFERENCES

- (1) Davis, C. H., and Colwell, C.: J. A. M. A. 92: 306, 1929. (2) Hesselting, H. C.: AM. J. OBST. & GYNEC. 26: 46, 1933. (3) Hibbert, J. F.: AM. J. OBST. & GYNEC. 25: 465, 1933. (4) Curtis, A. H.: Surg. Gynec. & Obst. 18: 299, 1914. (5) Kleegman, S. J.: Surg. Gynec. & Obst. 51: 552, 1930. (6) Davis, C. H.: AM. J. OBST. & GYNEC. 19: 575, 1929. (7) DeLee, J. B.: Illinois M. J. 37: 186, 1920. (7 A) Stein, I. F., and Cope, E. J.: AM. J. OBST. & GYNEC. 24: 348, 1932. (8) Greenhill, J. P.: AM. J. OBST. & GYNEC. 16: 870, 1928. (9) Goodall, J. R.: J. Canad. M. A. 25: 292, 1931. (10) Gellhorn, George: J. A. M. A. 100: 1765, 1933. (11) Wood, W. L., Jensen, L. B., and Post, Wilber E.: Ann. Int. Med. 8: 734, 1923. (12) Jensen, L. B.: J. Infect. Dis. 37: 481, 1926. (13) Rosenow, E. C.: J. Immunol. 26: 401, 1934. (14) Bumpus, H. C., and Meisser, J. G.: J. Urology 5: 249, 1921; also with Meisser, J. G.: Arch. Int. Med. 27: 326, 1921. (15) Bland, P. Brooke, Goldstein, L., Wenrich, D. H., and Weiner, Eleanor: Am. J. Hyg. 16: 492, 1932. (16) Rakoff, A. E.: Am. J. Hyg. 19: 502, 1934. (17) Rosenow, E. C.: Jordan and Falk's: The Newer Knowledge of Bacteriology and Immunology, Chicago, 1928, University of Chicago Press, p. 576. (18) Hegner, R.: J. Parasitol. 14: 261, 1928. (19) Hegner, Robert: Jordan and Falk's: The Newer Knowledge of Bacteriology and Immunology, Chicago, 1928, University of Chicago Press. (20) Smith, J. F.: Urol. & Cutan. Rev. 37: 615, 1933. (21) Wright, F. R.: Urol. & Cutan. Rev. 38: 335, 1933. (22) Waklin, O. S.: Svenska Lak-tidning 31: 137, 1934; Acta dermat.-Venereol. 15: 243, 1934. (23) Maxwell, E. J.: New England M. J. 27: 567, 1934. (24) Heckel, N. J., Jensen, L. B., and Wood, I. H.: J. Urol. 33: 284, 1935. (25) Cannon, P. R., and Sullivan, F. L.: Proc. Soc. Exper. Biol. & Med. 29: 517, 1932. (26) Culver, Harry: J. A. M. A. 103: 637, 1934. (27) Besredka, A.: Local Immunization, Baltimore, 1927, Williams and Wilkins Company,

## HYPOTHYROIDISM AS A PROBLEM IN WOMEN

## A BASAL METABOLISM STUDY OF 600 CASES

CARL HENRY DAVIS, M.D., MILWAUKEE, WIS.

**A**BNORMAL development of the thyroid gland, so frequently observed in the so-called goiter areas, presents many interesting medical problems. For centuries physicians have recognized that thyroid hypertrophy in women may occur as a congenital defect, or begin at puberty or during pregnancy. In Charpentier's *Cyclopedia of Obstetrics and Gynecology*, the American edition of which was published in 1887, there is a two-page discussion of goiter and its influence on pregnancy. Under treatment the writer of the article says: "As goiter is generally benign during pregnancy, we should resort to general measures and internal medication. Forbid the patient to nurse and give iodine."

Those of us living in goiter areas formerly accepted a moderate hypertrophy of the thyroid as an incident of pregnancy, and until Marine, in 1917, urged the use of iodine as a preventive measure, most of us who treat women patients gave the thyroid very little thought. Following Marine's advice, in 1920, I began administering iodine in some form to every obstetric patient who showed any hypertrophy of the thyroid. Later it was appreciated that all women living in goiter areas need the

iodine as a protective measure, and every pregnant woman under my care was advised to take it throughout the period of pregnancy. A review of my experience during the first years of this practice indicated that it was a mistake to stop the iodine following delivery, and since 1926 when my first paper on "Thyroid Hypertrophy and Pregnancy" was published, all patients have been advised to continue a reduced dose of iodine indefinitely. During the first years when the iodine was discontinued at delivery, ten patients in a total of 500 delivered returned with classic symptoms of toxic goiter within a year. Since having all patients continue the use of iodine, over 1,000 women have been carried through pregnancy and the puerperium, and to date not one has returned to me with evidence of toxic goiter. However, not all of them have been under periodic observation, and it is possible that such a condition may have been diagnosed elsewhere. Furthermore, not a single congenital hypertrophy of the thyroid has been observed since I have been giving iodine to all pregnant patients. It is evident that the prophylactic administration of iodine to pregnant women is effective in preventing hypertrophy of the thyroid of both mother and fetus. But will the iodine insure a normal development of the thyroid in the fetus of a woman who has hypothyroidism?

The problems associated with underfunction of the thyroid gland were, for many years, overshadowed by hypertrophy of the thyroid and thyrotoxicosis. Gradually it was appreciated that cretinism is not rare in America and that many women have varying degrees of hypothyroidism. DeQuervain, who has had an unusual opportunity to study cretinism, observes that cretins may be divided into two groups: (1) cretins with goiter, and (2) cretinoid dwarfs without goiter, but with an atrophic thyroid gland. He also furnishes evidence obtained by operation that the so-called infantile myxedema, a condition of dysfunction of the thyroid which may be noted first at school age, results from an absence of normal thyroid tissue, in his case there being only a small amount of accessory (sublingual) thyroid tissue which was not very active. The evidence available makes it appear doubtful if the mere administration of iodine to a pregnant woman with a fair degree of hypothyroidism will be sufficient to insure a normal development of the thyroid in the fetus. Many years must elapse before the clinical experiment with iodine, which is being conducted in Switzerland, will permit an answer to this important question. For the present it will be safer to assume that the hypothyroid woman who becomes pregnant should have thyroid medication as well as iodine.

However one may approach the thyroid problem, it becomes evident that control is best accomplished through prenatal care. Thus the real prophylaxis reverts to the physicians who are responsible for the care

of pregnant women. DeQuervain is convinced that the harmful changes which may result from improper development of the thyroid are evident by the seventh month of pregnancy, hence, administration of iodine and, when indicated, desiccated thyroid should be started as early as possible. There is some evidence to suggest that the definitely hypothyroid group should have this medication before the onset of pregnancy. But how are we to tell which women are in the hypothyroid group?

Myxedema, when well developed, should be recognized without difficulty, but most patients with moderate degrees of hypothyroidism do not show definite evidence of thickened skin or fluid retention. However, a considerable number have more or less constantly a slow pulse and a subnormal temperature. It has been our observation that practically all individuals who have the slow pulse and subnormal temperature have a low basal metabolism rate. While this is the best clinical indication that the patient may have a hypothyroidism, there is another group of women who may have an elevated pulse and a normal temperature, yet have a low basal metabolism rate and show marked improvement in their physical condition following the judicious administration of desiccated thyroid. If there is no clinical finding which will enable us to select all of the hypothyroid patients, are we not justified in using metabolism determinations routinely in our examination of women patients?

Preliminary to starting the routine basal metabolism rate in examination of women patients, we made a survey of the findings on all females tested in the laboratory at Columbia Hospital, Milwaukee, for a ten-year period ending Dec. 31, 1931. There were 1,205 women or girls who had one or more basal metabolism rate determinations with the following results:

Plus	55% and up	36	410 women or 34% above plus 10.
Plus	50-55	10	
Plus	45-50	23	
Plus	40-45	13	
Plus	35-40	31	
Plus	30-35	23	
Plus	25-30	31	
Plus	20-25	60	
Plus	15-20	95	
Plus	10-15	88	
<hr/>			
Plus	5-10	130	505 women or 42% in normal range.
Plus	0-5	110	
	0	21	
Minus	1-5	134	
Minus	5-10	110	
<hr/>			
Minus	10-15	114	290 women or 24% below minus 10.
Minus	15-20	77	
Minus	20-25	49	
Minus	25-30	22	
Minus	30-35	13	
Minus	35-40	4	
Minus	40 down	11	

Realizing that a hospital group would include a considerable number of patients who had been sent there with definite symptoms of toxic goiter, the ones whom I had referred to the laboratory for basal metabolism rate determinations were analyzed with the following results: In a total of 172 females with one or more checks there were 34 or 19.8 per cent with a basal metabolism rate above plus ten; a total of 91 or 52.9 per cent within the normal plus or minus ten, and 47 or 27.3 per cent below minus ten. The results of this analysis indicated that a considerable proportion of the women and girls living in Milwaukee and vicinity show abnormal basal metabolic determinations, and I concluded that routine determinations on a considerable series of patients coming to me for examination were justified. In an effort to avoid the criticism that this was adding unnecessary expense to the patient, the necessary laboratory equipment was secured, a competent technician employed, and a routine basal metabolism rate and complete blood count added to my regular general examination without making any additional charge to the patient, the former minimum being maintained. Only after need for repeated examinations had been demonstrated in any case was the cost of the subsequent determinations charged to the patient. The complete blood counts were of definite value, but it has not been possible to observe any relation between the blood count and the basal metabolism rate. The results obtained from routine basal metabolism rate determinations on a consecutive series of 600 females, some of whom have had a large number of tests, are shown in the following table:

Plus	30-35%	1	
Plus	25-30	5	
Plus	20-25	5	48 women or 8% above plus 10.
Plus	15-20	14	
Plus	10-15	23	
<hr/>			
Plus	5-10	34	
Plus	1-5	46	
	0	14	246 women or 41% in normal range.
Minus	1-5	58	
Minus	5-10	94	
<hr/>			
Minus	10-15	106	
Minus	15-20	98	
Minus	20-25	63	306 women or 51% below minus 10.
Minus	25-30	31	
Minus	30-35	7	
Minus	35-40	1	

A series of 100 pregnant women are included in the above analysis. They were grouped separately, and it was found that 18 per cent had readings above plus ten, 49 per cent within the normal plus or minus ten range, and 33 per cent were below minus ten. It will be noted that this pregnant group average very closely with the 172 patients whom I had tested at Columbia Hospital during the ten-year period.

The data presented indicate that a low basal metabolism rate is relatively common for women living in Milwaukee and vicinity. It is diffi-

cult to determine the percentage of the women with low rates who actually have a hypothyroid condition. The clinical test with the administration of desiccated thyroid is the only method which can be accepted at present, and it is difficult to keep patients under observation for long periods of time unless they are considerably upset from their varied symptoms. Nearly all of the women and girls with rates below minus ten were tested with small doses of desiccated thyroid, and with few exceptions they reported improvement in their general physical conditions and gradual correction of a wide variety of symptoms. A number of those with rates between minus 10 and 15 were found to have a perfectly normal rate after using 100 tablets ( $\frac{1}{2}$  gr. U. S. P.), and as their symptoms were relieved, the medication was discontinued with the instruction that they should return for another basal metabolism rate if further symptoms were noted. A few of these women who have been rechecked were found to have normal rates. On the other hand, it was observed that a goodly number of women showed a lower rate after their nervous condition became stabilized through the use of thyroid.

Interpretation of the basal metabolism rate, like other laboratory tests, may be difficult, except in cases where it confirms clinical findings or furnishes a clue to the thyroid as a factor in the cause of certain symptoms. It is generally recognized that an increased rate is not definite evidence of hyperthyroidism. A decreased rate is a more reliable evidence of thyroid deficiency, but it must always be remembered that this may be a temporary condition secondary to an infection or other cause, and that the thyroid function may be normal when the cause is removed. For this reason thyroid medication should be carefully controlled, even in patients who have evidence of myxedema.

The clinical results obtained following the administration of desiccated thyroid are more spectacular than those noted from most endocrine products. The numbers of patients treated by me do not justify conclusions, but I have found striking evidences of gynecologic problems in women with a low basal metabolism rate. These include uterine hemorrhage, sterility, repeated abortion, and premature labor. Hughes (1934) suggested that miscarriage and malformed babies may be more common in women who have a low basal metabolism rate. Four of the 100 pregnant women included in this study aborted, but only one was in the lower than minus 10 group with minus 14, two were within the normal limits, and one had a rate of plus 15. While this does not indicate any relation between basal metabolism rate and the abortion, during the past ten years I have had several patients with a low basal metabolism rate and had a history of repeated abortions who were able to go through a pregnancy after using thyroid medication. I have observed two women each of whom has delivered two congenitally de-

fective babies, and the only abnormal finding in each instance was a low basal metabolism rate. However, even though they should have normal infants after thyroid medication, we could not prove that the thyroid had made it possible.

A review of the symptoms and physical findings noted on the histories of our 306 patients who had a low basal metabolism rate shows that they have a feeling of fatigue or weakness and drowsiness in the majority of cases. In varying degrees they had all of the symptoms noted by Carey (1933) in the group studied in Minneapolis, namely, fatigue, weakness, drowsiness, generalized pains, joint pains, constipation, nervousness (depression, apprehension), menstrual disturbances, sterility, frequent miscarriages, overweight, dry skin, and falling out of hair (occasional). As previously stated, it is evident that women who have a dry skin, subnormal temperature, and slow pulse practically always have a low basal metabolism rate. Very often those who complain of weakness and drowsiness or excessive fatigue without any physical findings suggestive of hypothyroidism have a low rate temporarily, but return to normal after using thyroid medication for some weeks, and thereafter may continue normal for long periods. It is not possible at present to predict the future for this latter group, although one may suspect that as they grow older a considerable number will show other evidence of hypothyroidism.

A comparison of the percentages obtained in this study with earlier observations on pregnant women reported by me in 1926 suggests that there is a marked increase in the number of Milwaukee women who have a low basal metabolism rate. A reduction is also noted in the frequency of hyperthyroidism. Several explanations might be suggested, but they are all hypothetical. Each generation living in a goiter area may be expected to show more evidence of deficiency unless careful prophylactic measures are instituted. The more general use of iodized salt or iodine in other form apparently has reduced the incidence of thyroid hypertrophy and toxic goiter in this area. It is possible that more individuals with deficient thyroids are now passing over to a state of clinical hypothyroidism without first showing evidence of thyrotoxicosis. Certainly this study of 600 women and girls indicates that a low basal metabolism rate is a common condition in the Milwaukee area and justifies including this test in all general examinations. If one-third of all pregnant women in this area do have a low rate, it is evident that a considerable group of infants may show thyroid deficiency within a few years after birth unless the mothers use thyroid medication during pregnancy. It must be admitted that we have no definite proof at present that the use of desiccated thyroid and iodine will enable the woman with a thyroid deficiency to deliver an infant who will have a normal gland, but this medication should increase the percentage of normal infants. Our



present knowledge of the thyroid problem indicates that it must be corrected through adequate medication previous to pregnancy and during the early developmental intrauterine life of the fetus. Therefore, it is evident that prevention of thyroid disease is dependent upon measures which must be instituted by the physicians who care for women during pregnancy.

There is considerable difference of opinion regarding the amount of iodine which should be administered as well as the best means for supplying it. DeQuervain, in 1932, wrote as follows: "The iodized salt dispensed in Switzerland contains so much iodine that its daily use adds 0.5 mg. to the amounts otherwise supplied. This prophylaxis proves efficacious, and is entirely harmless. Occasional untoward reactions are of a transitory nature. But the conclusions drawn from this nationwide experiment, which is the Swiss iodine prophylaxis, will not be final before a generation treated systematically from mother's womb to the twentieth year of life is subjected to an equally systematic medical control, which will be in about twenty years." He believes that the dose of iodine used in America (2 mg. per day or more) would be dangerous in a region where goiter is endemic, but suggests that larger doses may be used for intrauterine prophylaxis and during childhood. It has been my practice to administer five minims of the syrup of hydriodic acid every other day during pregnancy, or if preferred, an iodostarine tablet three times per week. Following delivery the patient is advised to use iodized salt, and to continue to take the syrup of hydriodic acid or iodostarine each Sunday. As previously stated, over 1,000 patients have been delivered since starting this plan, and not one has returned with any evidence of hyperthyroidism.

If a patient has a low basal metabolism rate, I am accustomed to start with a small dose of desiccated thyroid, varying the amount with the basal metabolism rate, and to increase or decrease the dose according to the subsequent determinations. In every case the smallest dose which will carry the patient is employed. As the dose of thyroid preparations varies, it is important that patients be continued on the product of a single manufacturer. To insure fresh tablets of a uniform material, I have discontinued writing prescriptions for thyroid, and now dispense the tablets just as is done with other gland products which must be administered with the hypodermic. The administration of desiccated thyroid when checked with basal metabolism rate determinations should be free from danger.

## TOXEMIA OF PREGNANCY

J. R. GOODALL, M.D., MONTREAL, CANADA

*(From the Obstetric Service of the Royal Victoria Hospital)*

THERE is but one toxemia during the second and third trimesters of pregnancy. Its clinical manifestations, however, are very numerous; this variety of symptoms is constitutional, therefore dependent upon the individual, and more particularly upon which one of the various systems bears the brunt of the attack, and develops the high lights of the clinical picture.

All toxemic cases can be placed in two great categories, the acute and the chronic. These will be elaborated fully. It may be stated here for emphasis, for further emphasis later, that what the acute case is in symptomatology, the chronic is not; and that in their destructive processes these two differ as greatly as do acute pneumonic infections from chronic infective infiltrations; in fact, the parallel is perfect in most of the particulars.

Acute cases of toxemia have been greatly reduced by the observations of antenatal clinics. But per contra, the chronic cases have not fallen in their incidence, and outnumber the acute cases about fifty to one. Next to finding a specific for toxemia, it must be our chief clinical endeavor to detect the early "larval" stages of the disease. These are usually amenable to treatment. Every mutation of the internal milieu is an accommodation. As a consequence, acute intoxications are dangerous in proportion to their acuteness, because the body cells and their specific functions cannot accommodate themselves to their new environment. Time, and time only, is necessary to permit mutation for accommodation to take place. Hence the relative paucity of eclamptic seizures in chronic cases, and the more prolonged the toxemia, without acute exacerbations, the less is the danger of a cataclysmic discharge.

Blood changes, as elicited by chemical analysis, are the result and not the cause of the toxemia, and are of very little help in the differentiation of those patients who will become chronic nephritides from those in whom there will be no residual diminution of renal capacity. When retention products are chemically recognizable in the blood, the cases are usually easily recognizable clinically as having passed from the stage of "nephrosis" to that of "nephritis."

There are great differences in susceptibility to eclampsia and toxemia, in the age and temperament of patients; and familial factors play an important part.

Our vision as regards the effects of toxemia upon the mother and offspring is too restricted. This is a plea for a long vision study, particularly the study of the child born of a toxic mother, as to its subsequent development to adolescence and maturity. The views of pediatricists differ very widely upon this subject.

Last, this paper will deal in a very cursory way with placental pathology in relation to toxemia. Toxemia and its appended placental pathology is the subject of an exhaustive study which will appear shortly. This paper is a very brief abstract of this monograph. Placental pathology is almost a virgin field and the placenta at term is a veritable museum of abnormal processes. These changes are facts, indisputable, irrefutable; their interpretation into clinical causes is, as yet, chiefly by inference.

#### CHARACTERS OF TOXEMIA

Though there is but one toxemia of the late trimesters, one finds that the cases have many clinical manifestations and manifestly, therefore, the proteanicy of the clinical symptomatology must reside within the patient and be constitutional in origin. The clinical picture will depend upon the patient's system that shows the least accommodation to the new toxic environment. The determination of the affected system will depend upon individual instabilities, or low reserve, or specificity in elimination of the poison, or a combination of two or more of these factors. One can readily see how each of these may operate to the detriment of the patient. An unstable nervous or vascular system will show that instability, under the stress of change, incident to a toxic state; the former, in a predisposition to nervous symptoms, and an easy accession to eclampsia; in the latter, to vascular extravasations in the form of edemas, local or general, and hemorrhagic states. Then again, should a large number of kidney tubules and glomeruli have suffered from some antecedent disease and renal reserve consequently be lowered, one can readily understand the establishment of a renal block under the stress of eliminating either a foreign product or a concentrate.

#### CLINICAL TYPES OF TOXEMIA

Clinically cases may be divided into acute and chronic. This subdivision, though arbitrary, is extremely useful. It is arbitrary because there are intermediate cases which are neither acute nor chronic; and useful, because the acute and the chronic differ so fundamentally, not only in symptomatology, but also in sequelae, and destructiveness of function, that acute and chronic cases stand to each other in nature of a contrast.

The acute case, like acute lobar pneumonia or any other acute infective invasion, is quickly over, leaving usually a minimal unrecognizable

loss of function after recovery and a reserve capacity that seems, to our imperfect methods of examination, to be unimpaired. But contrast the destructive effect of a chronic lung or other organ infection, its fibrosis, its incidence to the tissue's endeavor to circumscribe the infection, and contrast the consequent loss of functional capacity. The parallel, in this respect, between the acute and chronic toxemias of pregnancy, on the one hand, and that of similar states of infection, is perfect in almost every detail. On the one hand, toxemias, if they do not destroy the patient by virtue of their acuteness, may not impair the patient's powers of procreation in the slightest degree. This is such a common observation that it requires no further elaboration. On the other hand, chronic cases, by virtue of their duration and low intensity, permit a certain corporeal adjustment, an accommodation of cell function to a new internal environment, but function nevertheless, under these new circumstances, means cell stress and that, if prolonged, spells permanent exhaustion and lack of power of recuperation. That state causes decompensation, and therefore *recognizable* pathology, as distinguished from *unrecognized* pathology, which is not apparent because the cells have not fully lost their compensation, and are still operating within their reserve limits. A problem at once presents itself. The popular subdivision of diseases into functional and organic still holds sway, but it has grown very threadbare. The wider science opens the doors into medical dark chambers, the more restricted becomes the number of functional diseases. It is a term used to cover our lack of knowledge. Rather let us realize that functional and organic changes are always synchronous, and that the former are the outward and clinical signs of an inward and organic lack of accommodation to a new environment. Every physical, every chemical change in the human body is an attempt at accommodation and where that accommodation fails, there we have the initiation of the steps that can lead only to extinction of the individual or race.

But just as acute cases leave a minimum of sequelae as contrasted with chronic cases, so are acute cases dangerous by virtue of the suddenness of the changes to which the body has to conform or it must inevitably succumb. So that acute toxemias, like acute infections, are short lived, intense, startling in symptomatology, often destructive of the individual by toxicity, but not destructive of separate systems. Chronic cases, on the other hand, are seldom destructive of the individual by their toxicity, but by system changes and consequent progressive perverted metabolic function. The destructive properties of the chronic cases can be measured by the equation, intensity multiplied by chronicity on the one side, and individual reserve on the other.

Acute cases fall readily into four clinical groups: (1) Renal, (2) hepatic, (3) extravasatory, and (4) neural. These subdivisions have been fully dealt with in my previous papers and require no further

elaboration except that their relative incidence is approximately as follows: 20 renal types to 2 hepatic to 10 extravasatory to 1 neural. The prognosis fortunately is inversely as their incidence. That is, the neural type claims the highest mortality rate, the hepatic next, the hemorrhagic follows, and the renal has the lowest mortality.

#### BLOOD CHEMISTRY

The work of studying 300 cases, where blood chemistry was done at least once, or several times during the height of the disease, has proved most enlightening. The variation in blood contents has almost invariably been within normal limits. When, on the other hand, there were evidences of retention in the blood, the cases could usually easily be diagnosed clinically as having passed from a nephrosis to a nephritis. The transition is usually slow and insidious and may not be apparent except under stress. Moreover, it is worthy of our attention that retention products in the blood must not be taken at face value. They are estimable only when taken in conjunction with the patient's history and present condition. The importance of this cannot be overstressed.

There is now in the hospital a woman, sixty-eight years of age. Twenty years ago she had a blood pressure of over 200, taken at several times over a long period. She was told then, after careful clinical and chemical examinations during hospitalization, that she would probably live six months, not more. This was the prognosis of one of the best professors of clinical medicine. She is now under observation with a blood pressure of 240 over 120, and this has never been found below the 200 line at any taking in the past twenty-two years. Her blood chemistry shows an unusually high retention as follows:

Creatinine varies between 4 and 7.36; nonprotein nitrogen varies between 78.4 and 112; urea nitrogen varies between 50 and 81 on repeated examination, and yet the patient is exceptionally well, symptom-free, and capable of doing her ordinary daily round without discomfort.

This case is quoted fully, to illustrate the influence of time in allowing accommodation of cell function to a slowly changing internal milieu. There is probably not any woman who could live with the above quoted chemistry, were the process at all acute, or even subacute. So all values in medicine are relative. The time element is a very weighty factor. It is the time element that determines the differences in symptomatology and the more striking differences in pathology between the acute and the chronic cases.

Another factor to which little or no attention has been given is the individual and familial susceptibility to toxemia and, in particular, to eclampsia. Age is an important factor. In the past eighteen months there have been three cases of eclampsia in girls about sixteen years of age. The seizures were not severe, subsequent coma was short, and the patients were clinically not very toxic. They all recovered without appreciable damage. The percentage of such cases was *very* high as com-

pared with that of older women. The inference is clear that the child's nervous system is more susceptible to nervous explosions than is the more hardened adult. I have had two cases of eclampsia in my own private practice in the past fifteen years. Both of these were morons, veritable children mentally; they both went into convulsions during labor; the convulsions were mild, and short. One had to be transferred to a mental hospital during her puerperium, and has never recovered her normal state of vegetative sanity; the other will probably produce a long list of moronic descendants. This instability and explosive tendency of children is seen clearly in infections, where chills take the place of convulsions. So it is with high strung neurasthenic and hysterical women. They are virtually children in their nervous instability. Time and its thundering impulses have not hardened the nervous system. The alloy is not susceptible to tempering. On the other hand, beware of the woman whose mother has taught her emotional control in her childhood, and who had practiced it in subsequent years. She will not become convulsive until her nervous system becomes saturated, and the union of the toxic agent and the nervous cell may become so intimate as to defy a restoration. If recovery takes place, the nervous sequelae are often severe, distressing, and protracted.

#### THE EFFECTS OF TOXEMIA UPON THE OFFSPRING

No one who has seen the effects of chronic toxemia upon the newborn can but be impressed by its seriousness. Since the placenta suffers so much (as will be shown later) from the agents of toxemia, is it natural to assume that the child, of which the placenta is merely an appendage, could be invulnerable? When we consider that all degrees of placental disease, up to the degree of complete sequestration, can occur, is it tenable that the child could escape its effects? Experience teaches us the contrary. If so, then what is the subsequent history of these children? Are they low in system or organ reserve? How do they stand the major diseases of childhood? What is their history as men and women? What is the effect of procreation in women with a history of toxemia in their prenatal life? Pediatricians differ markedly in their reaction to these questions. That is not surprising. It is only in the past few years that this long vision has come into consideration. What is surprising, however, is that one experienced specialist, who has had sad personal experiences, states that they are all below par and most of them die before reaching five years of age. Others equally emphatic minimize the effects of maternal toxemia upon the offspring. The truth, like all truth, is halfway between these extremes. The degree and the duration of the toxemia are factors beyond the ken of the pediatrician, yet these are the dominant factors, and these are known only to the experienced and observing obstetrician. This question of child-effect must demand our most careful and prolonged attention.

## PLACENTAL DISEASE

This is almost a new and virgin field of pathology. There issues from its careful study the following diseases, some new, others with a new significance. In the order of their frequency they are: (1) chorionic sclerosis, (2) placentosis, (3) hemorrhages, and (4) degeneration cysts.

Underlying all these, there is a common fundamental cause, toxemia, and a predisposing factor, senility. Every placenta lives the stages of life common to all living things. It has its embryonic period, its childhood, its adolescence, its maturity and its senility. Ordinarily senile predispositions begin about the seventh month. The causes for this were outlined in a previous paper. In other instances senility may be tremendously advanced or somewhat delayed. These are the exceptions. Senility predisposes to a preternatural susceptibility to toxic changes, just as old age in the individual inflicts a narrowing range of physical and chemical liberty.

Toxemia, on the other hand, is a change in the internal milieu of the pregnant mother, and the acuteness or chronicity of that change determines not only the symptomatology, as previously emphasized, but also the pathology. Acute toxic states of short duration show a minimum of placental change, only a short-lived, variable placentosis. Chronic toxic states produce placental changes of a profound character akin to that of chronic inflammatory lesions of the lungs, where all the lesions enumerated above may coexist, in variable degrees, even to the degree of almost complete exclusion of one or more. The insidious extension of any one of these may so impair the function of the placenta as to jeopardize the life of the child. Of chorionic sclerosis and its effect upon restricting the extension of the chorionic plate, I have written fully quite recently. Placentosis, on the other hand, is a new disease. It is acute, or less acute, or chronic. The acute stages are rare and very short lived. The placenta, when so affected, is of a bluish black color, engorged, the fetal vessels are tremendously distended, the cotyledons are swollen and rounded as if under tension. When cut, the placenta oozes almost black blood. When hardened and cut in slices, there are hemorrhages scattered through the placenta, but unless extensive, these are more or less confined to the center of the cotyledons. This is spoken of as the stage of red hepatization, owing to its resemblance to a lung in that pathologic state. Microscopically, the fetal blood vessels are so engorged that their walls are almost invisible, and fetal extravasations of blood are visible in every field. This condition is not a result of labor, for it occurs just as frequently in section cases. This state, if it lasts several days, may lead to complete sequestration of the placenta and, if it be retained a few days, it will be cast off as a huge yellow placenta, in which fatty degeneration is the dominant change.

If, on the other hand, the child should survive, the placenta may undergo complete resolution and leave very few traces of placentosis. If, however, the recovery is slow, it presents a characteristic change. The placenta cuts as, and has the appearance of, a lung under gray hepatization. It cuts in a ragged way after hardening and there is a distinct alveolation, in which the differentiation between cotyledons and maternal intercotyledonous tissue is easily made out. The intercotyledonous tissue is edematous, soft and ragged. The cotyledons are of firmer consistency. The cotyledons recover from the periphery, leaving a central hemorrhage or cavity (alveolation). Placentas may recover in part, other parts may go under sequestration. This will depend upon the site of the placenta and its consequent blood supply. Similarly, in multiple pregnancies, one child may die, while the others may survive. Life depends upon such seemingly insignificant details.

Placentosis in its insidious, more or less chronic, stage may show coincident advances in one area, and imperfect reparation in another. This complicates the picture to a puzzling degree. There is a subtle connection between placentosis and the onset of labor, which will be dealt with in my larger monograph.

Placental hemorrhage is one of the commonest of placental diseases. In the 750 placentas so far examined, there were over 500 cases of macroscopically recognizable hemorrhage. These varied in size from millet seeds to oranges. In only eleven of these was the condition recognized clinically either ante- or intrapartum. It can definitely be established by my studies that this condition is another of the many placental manifestations of a general toxemia. That the placenta is chosen for the baneful changes incidental to toxic states, is in accordance with two distinct biologic factors, first, the law of selectivity, and second, the greater susceptibility of the placenta, because it is a mushroom growth, imperfect in development, short lived, and consequently vulnerable.

Degeneration cysts are found only in the maternal intercotyledonous tissues. They begin as a hyaline swelling and degeneration of the decidual cells very similar to the swelling and hyaline degeneration of uterine tissues postpartum, as described in my monograph upon regeneration of uterine vessels in the puerperium. The centers of these degenerated masses become gelatinized and homogeneous and of a pale green color, or in a less perfect state, the central part contains bizarre phantoms of the swollen cells. The walls are always made up of decidual cells in various stages of degeneration. These cysts are extremely common, affecting about 25 per cent of placentas at full term, and may vary in size from a millet seed to an almond. They have no clinical significance except as an index of degeneration and, when present, they are usually of all sizes and numbers.



## OVARY-STIMULATING FACTORS AND ANTIHORMONES\*

C. F. FLUHMANN, M.D., SAN FRANCISCO, CALIF.

(From the Department of Obstetrics and Gynecology, Stanford University School of Medicine)

THE recent discovery that the prolonged administration of gonadotropic hormones to laboratory animals leads to the production of inhibiting substances may prove an important advance in our knowledge of the physiology of sex hormones. It has been recognized for some time<sup>1, 2, 3</sup> that the continued daily injection of laboratory animals with gonadotropic extracts from pregnancy urine or placenta or from anterior pituitary material, leads first to a great increase in the size of the ovaries, but subsequently there results a loss of the gonad-stimulating effect and an actual regression of ovarian weight. It remained for Collip and his collaborators<sup>4, 5, 6</sup> to show that this regression is not due to ovarian failure, because animals injected with chorionic hormone preparations are still able to respond to pituitary extracts and vice versa. For instance, animals given a placental extract (A-P-L) eventually reach a stage where the ovaries not only fail to increase further in size but actually diminish to less than normal weight, and the administration of pituitary preparations at this time still elicits a response. They also noted that the regression of the ovaries of the injected animals is due to the production of certain substances which have the power of completely inhibiting the action of the hormone employed. This can be demonstrated by the fact that extracts mixed in vitro with serum from treated animals become inert, and that a passive resistance can be induced in rats by the injection of such serum. Since this work may possibly find important clinical applications, the present study was conducted to determine some of the properties of such "antihormones" and the conditions under which they may be produced.

### TECHNICAL PROCEDURES

The technical procedures employed in the Stanford Gynecological Laboratory and details regarding the animals, their age at maturity, the method of estimating organ weights and their percentage of increases, and the standardized way in which the extracts are administered, have been fully described in a number of previous communications.<sup>7, 8, 9, 10, 11</sup> In experiments of long duration control

\*Supported in part by the Rockefeller Fluid Research Fund of Stanford University School of Medicine. The sheep anterior pituitary material was generously donated by Parke, Davis and Company through the courtesy of Dr. E. A. Sharp. My thanks are also due to Dr. D. A. Wood and members of the Department of Pathology for the human anterior pituitary glands from autopsy material, and to Mr. John J. Kan and Mr. Pierre Lassegues for their faithful technical assistance.

figures for organ weights were obtained for this study from groups of seven or more normal rats sacrificed at 51, 82, 111, and 141 days of age. The method of preparation of ovary-stimulating extracts from blood of pregnant women has also been given before.<sup>7, 10</sup> It is based on the work of Wallen-Lawrence and van Dyke,<sup>12</sup> and depends on an alcohol precipitation of citrated blood, extraction of the precipitate with a sodium-acetate-acetic acid buffer, pH 4.2 to 4.5, and reprecipitation of the active material with 95 per cent ethyl alcohol. The human anterior lobe extracts were prepared from autopsy material obtained from patients of both sexes and of all ages. The fresh glands were cut into small fragments and kept in acetone for several days or weeks, and were finally dried in vacuo at room temperature. They were then ground up, and the resultant powder extracted in the same way as that used for making extracts from blood of pregnant women.

The method of testing for the "antihormone" property of the serums of injected animals was similar to that first employed by Collip and Anderson<sup>13</sup> in studying the antithyrotropic hormone. A mixture of equal amounts of serum and one of the extracts was injected into groups of immature rats. It was given twice daily in 0.5 c.c. doses for four days, and the rats were sacrificed in 120 hours. The potency of the extracts used is not given in rat units but was determined by injecting control series of rats with a mixture of the same preparation and an equal amount of serum from normal animals. It was thus possible to compare directly the effects induced in 120 hours in the ovaries of immature rats.

## RESULTS

*Human Pituitary Extract.*—The first series of experiments consisted in the daily injection of a small dose of human pituitary gonadotropic extract to immature rats 21 to 23 days of age. A total of 39 animals was used for this purpose, and the injections were continued for as long as 119 days. Seventeen rats were autopsied in 5 days, while 6 were sacrificed in 30 days, 6 in 61 days, 6 in 90 days, and 10 in 119 days. In addition, 20 rats were treated for 119 days, and were then injected for 5 days with either sheep pituitary extract or pregnancy blood extract.

The effect of such injections on ovarian weight is shown in Fig. 1. In 5 days the ovaries had increased 50 per cent over the weight of the control animals, and in 30 days the increase was 86 per cent, but after treatment for 61 days, the ovarian weight was equal to that of the controls, while in 90 and 119 days it had actually diminished 26 and 19 per cent.

The serum of the rats injected for 90 and 119 days was examined in the manner described in the preceding section for the presence of any "antihormones." As shown in Table I, it was found to possess a great inhibiting power toward extracts prepared from human pituitary gland material. For instance, Extract 55 mixed with an equal amount of serum from normal animals was able to induce a 618 per cent increase in ovarian weight of immature rats over a five-day period. On the other hand, the ovaries of young rats injected in the same manner and with the same extract but mixed with serum from animals treated previously for 90 days, failed to show any response and actually weighed 10 per cent less than those of normal controls.

In contrast to the definite "antihormone" property of this serum as regards human pituitary extracts, it was now found that it was unable to inhibit the action of preparations made in the same way from sheep hypophyses. A mixture

of sheep pituitary extract and the serum from the injected rats produced an increase in ovarian weight of 300 per cent, whereas the same extract mixed with normal rat serum resulted in a 210 per cent increase.

A remarkable finding, however, was the fact that the serum of the rats injected for long periods of time with human pituitary extract had "antihormone" properties toward the chorionic gonadotropic hormone. A mixture of normal rat serum and pregnancy blood gonadotropic Extract 26 was able in five days to cause a 190 per cent increase in ovarian weight, and histologic examination showed the presence of corpora lutea, lutein cysts, and developing follicles. On the other hand, the same extract mixed with an equal amount of serum from the experimental rats induced no increase in the weight of the ovaries which histologically gave the picture seen in normal immature rats.

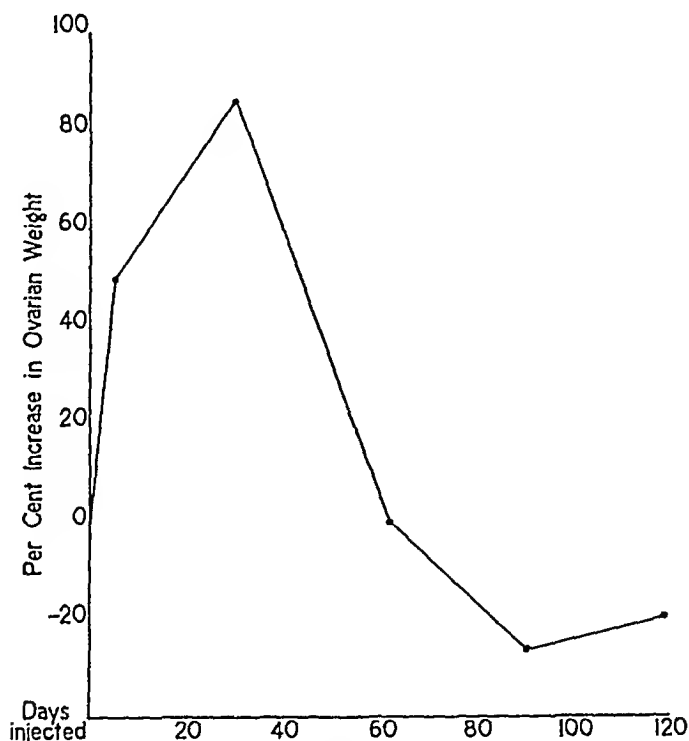


Fig. 1.

Since the ovaries of rats injected for 119 days with a human pituitary extract weighed less than those of normal controls, it seemed of importance to repeat the experiment of Selye and others<sup>4</sup> and determine whether they could still respond to other preparations. Ten rats treated in this way thus received two injections daily of a sheep pituitary extract and were sacrificed in five days. It was seen that the ovaries were still capable of responding and showed a 61 per cent increase in weight. A second series of 10 similar rats were given two daily injections of a pregnancy blood extract, but in five days the ovaries showed only a slight increase (23 per cent). The blood serum of the rats used in these experiments also showed the presence of "antihormones" effective against human pituitary and pregnancy blood extracts.

*Chorionic Gonadotropic Hormone.*—The injection of pregnancy blood extract to rats over a long period of time in order to stimulate the formation of antihormone has met with a number of technical difficulties. These experiments are

therefore incomplete and must be reported at a later date. However, in keeping with the work of Twombly and Ferguson<sup>14</sup> and Bachman, Collip and Selye,<sup>15</sup> it has been found that inhibiting substances readily form in the rabbit.

Two rabbits were injected once daily with a gonadotropic pregnancy blood extract for periods of forty-two and seventy-four days, respectively. At the end of that time the animals were sacrificed and the blood serum examined for the presence of antihormones.

TABLE I. THE DEMONSTRATION OF ANTIHORMONE PROPERTIES IN THE BLOOD SERUM OF RATS INJECTED FOR A LONG PERIOD OF TIME WITH A HUMAN PITUITARY GONADOTROPIC EXTRACT

	NUMBER OF RATS	AVERAGE BODY WT.	GROSS WEIGHTS		PER CENT INCREASE OVARIAN WEIGHT
			UTERUS	OVARIES	
H.P.E.* No. 55 plus N	3	28	0.072	0.082	618
H.P.E. No. 55 plus H	4	42	0.029	0.013	-10
H.P.E. No. 57 plus N	4	29	0.055	0.026	118
H.P.E. No. 57 plus H	4	28	0.063	0.009	-23
S.P.E. No. 50 plus N	5	35	0.053	0.037	210
S.P.E. No. 50 plus H	5	39	0.059	0.052	300
P.B.E. No. 25 plus N	5	27	0.103	0.020	72
P.B.E. No. 25 plus H	4	39	0.081	0.010	-20
P.B.E. No. 26 plus N	4	37	0.136	0.038	190
P.B.E. No. 26 plus H	4	43	0.035	0.015	0

\*H, Serum from rats injected daily with a human pituitary extract for 90 or 119 days.

N, Serum from normal control rats.

H.P.E., Human pituitary extract.

S.P.E., Sheep pituitary extract.

P.B.E., Pregnancy blood gonadotropic extract.

As shown in Table II, the serum from the injected rabbits was able to render pregnancy blood extracts ineffective. Pregnancy blood Extract 313 mixed with serum from a normal rabbit induced a 155 per cent increase in the weight of the ovaries of immature rats, while the same preparation mixed with serum from the animal injected 74 days gave only a 40 per cent increase.

On the other hand, the serum was unable to inhibit extracts prepared from either human or sheep pituitary glands. The "antihormone" property developed by the rabbit serum was thus effective only against the chorionic gonadotropic hormone.

*Blood of Postpartum Patients.*—During pregnancy in the human being, there is a constant production and excretion of a very active gonadotropic substance which is readily demonstrable in the blood and urine but which rapidly disappears after delivery. Since Bachman and his collaborators<sup>15</sup> have shown that antihormones may persist for a long time after the cessation of treatments in experimental animals, it seemed that the puerperal woman presented a unique opportunity to determine if inhibiting substances are formed under the stimulus of a hormone produced by an individual in physiologic conditions.

The blood of four patients from five to nine days postpartum was first examined and found to be free of chorionic gonadotropic factors. It was then

mixed in equal amounts with a pregnancy blood extract or with a human pituitary gland preparation and tested for the presence of antihormones as in the

TABLE II. THE DEMONSTRATION OF ANTIHORMONE PROPERTIES IN THE BLOOD SERUM OF RABBITS INJECTED FOR A LONG PERIOD OF TIME WITH A PREGNANCY BLOOD GONADOTROPIC EXTRACT

	NUMBER OF RATS	AVERAGE BODY WT.	GROSS WEIGHTS		PER CENT INCREASE OVARIAN WEIGHT
			UTERUS	OVARIES	
H.P.E.* No. 64 plus N	3	41	0.104	0.089	540
H.P.E. No. 64 plus R	3	20	0.090	0.049	427
S.P.E. No. 70 plus N	3	24	0.064	0.041	340
S.P.E. No. 70 plus R	2	30	0.067	0.095	682
P.B.E. No. 31 plus N	3	29	0.114	0.025	190
P.B.E. No. 31 plus R	3	25	0.076	0.015	30
P.B.E. No. 313 plus N	3	27	0.086	0.031	155
P.B.E. No. 313 plus R	3	34	0.024	0.016	40

\*R, Serum from rabbit injected for 74 days with a pregnancy blood gonadotropic extract.

N, Serum from normal control rabbits.

H.P.E., Human pituitary extract.

S.P.E., Sheep pituitary extract.

P.B.E., Pregnancy blood gonadotropic extract.

previous experiments. In no instance could these be demonstrated by this means, and it would thus seem that inhibiting substances do not form in the pregnant woman in spite of the constant excessive production of the chorionic gonadotropic factors for the whole duration of gestation.

#### COMMENT

The experiments reported in this study corroborate the finding of Collip and his collaborators that the prolonged administration of gonadotropic extracts leads to the production of substances capable of inhibiting the action of similar preparations. There is, however, a definite species-specificity as regards the formation of these substances, and it is as yet uncertain whether definite "antihormones" are formed or whether the inhibition can be attributed to an immunologic reaction.

From the standpoint of the clinician, two observations are worthy of note. In the first place, it is yet uncertain that "antigonadotropic hormones" will prove of great importance in the study of various pathologic conditions associated with menstrual disorders. At any rate, it will first be necessary to demonstrate that they may be produced under the stimulus of hormones normally present in an individual. Second, the formation of such substances in experimental animals requires a prolonged course of treatment. It seems doubtful, therefore, that the present clinical usage of active gonadotropic extracts could lead to the same result, although this problem is open to experimental investigation.

# SUMMARY

A series of experiments has been conducted to study the occurrence of "antihormones" in the blood of experimental animals injected daily for a long period of time with gonadotropic extracts.

The injection into rats of a preparation of human pituitary gland for 90 or 119 days resulted in the production of substances capable of inhibiting the action of gonadotropic extracts prepared from both human hypophyses and from blood of pregnant women. A species-specificity was demonstrable, however, as it proved ineffective with sheep pituitary extracts.

The administration to rabbits of a human pregnancy blood gonadotropic extract for seventy-four days resulted in the production of substances capable of inhibiting similar extracts, but ineffective against either human or sheep pituitary gland preparations.

It was not possible by similar means to demonstrate any "antihormones" in the blood of women during the first ten days of the puerperium.

# REFERENCES

- (1) Zondek, B.: Die Hormone des Ovariums und des Hypophysenvorderlappens, Berlin, 1931, Julius Springer. (2) Collip, J. B.: Internat. Clin. 4: 51, 1932. (3) McPhail, M. K.: J. Physiol. 80: 105, 1933. (4) Selye, H., Collip, J. B., and Thomson, D. L.: Proc. Soc. Exper. Biol. & Med. 31: 487, 1934. (5) Idem: 31: 566, 1934. (6) Collip, J. B.: J. Mt. Sinai Hosp. 1: 28, 1934. (7) Fluhmann, C. F.: Proc. Soc. Exper. Biol. & Med. 29: 1193, 1932. (8) Idem: 30: 147, 1932. (9) Idem: 30: 881, 1933. (10) Idem: Endocrinology 17: 550, 1933. (11) Idem: Am. J. Physiol. 106: 238, 1933. (12) Wallen-Lawrence, Z., and van Dyke, H. B.: J. Pharmacol. & Exper. Therap. 43: 93, 1931. (13) Collip, J. B., and Anderson, E. M.: Lancet, p. 76, 1934. (14) Twombly, G. H., and Ferguson, R. S.: Proc. Soc. Exper. Biol. & Med. 32: 69, 1934. (15) Bachman, C., Collip, J. B., and Selye, H.: Ibid. 32: 544, 1934.

STANFORD UNIVERSITY HOSPITAL

---

Puhr, L.: The Pathogenesis of Krukenberg Tumors, Monatschr. f. Geburtsh. u. Gynäk. 99: 229, 1935.

The author emphasizes the rarity of Krukenberg tumors. During the last seventeen years only three cases were encountered in the Second Woman's Clinic at Budapest. He reports a case where the lesions were limited to the mucous membranes, chiefly those of the bronchi, stomach, gallbladder, common duct and the urethra. However, other organs were infiltrated, including the ovaries, liver, lungs, adrenals, lymph glands and bones.

J. P. GREENHILL.

## RECENT ADVANCES IN HYSTEROGRAPHY

THOMAS O. MENEES, M.D., AND J. DUANE MILLER, M.D.,  
GRAND RAPIDS, MICH.

MOST of the previous roentgen studies of the uterus have been made during the course of investigations for tubal patency. This has been done, for the greater part, with iodized oils which have yielded very satisfactory shadows, indicating the size, shape, and tonicity of the uterus. Sometimes intrauterine lesions were demonstrated. The method, therefore, was extended to the investigation of the uterus itself. However, on complete filling of the cavity with contrast material, the density of the medium was so great that small lesions were often obscured or the irregularities of contour obliterated by the pressure employed. Some technical difficulties were occasionally experienced in keeping the medium in the uterus while changing the patient's position. Also, there were certain dangers attending its use when recent bleeding had occurred. Last year we reported the development of a contrast medium for the roentgen demonstration of the relief of the endometrium.

A thorium hydroxide solution has been used for this purpose. On contact with alkaline mucus the solution is converted to a gel which adheres to the surface, thus applying a radiopaque coating.

We have used the following technic: The patient is placed in stirrups. After soap and water preparation, a bimanual examination is made to rule out pregnancy and active pelvic inflammatory disease. A large bivalve speculum is inserted, the cervix cleansed with alcohol, and the posterior lip grasped with a tenaculum. Two or three small graduated dilators are passed, dilating the cervix sufficiently to insure a free return of fluid around the cannula. About 20 c.c. of the medium are slowly injected into the uterine cavity allowing the excess to run back into the vagina as injection proceeds. The cannula is then removed and the remaining material wiped from the vault with gauze. It is advantageous to leave the coagulum adhering to the portio. The speculum is removed leaving the tenaculum in place and the patient transferred to the radiologic table. One anteroposterior film is taken on the Potter-Bucky diaphragm and developed at once. A sufficient quantity of contrast material usually adheres to the endometrium to cast a satisfactory shadow on the film. Occasionally the shadow is too faint and the injection must be repeated; or too dense, in which case expulsion of the excess can be promoted by allowing the patient to walk about for a few minutes. If the film is satisfactory, right and left oblique and postero-anterior exposures are made.

The roentgenograms constitute a record of the surface markings of the endometrium and show a considerable amount of detail previously unobtainable.

Examination of a normal uterus in this manner shows:

1. The contour of the uterine cavity.
2. The surface markings of the endometrium. These produce a mottled or finely latticed appearance when the examination is made shortly after menstruation. As the cycle progresses the markings become coarse and the endometrium is thrown into longitudinal folds.
3. The cervical canal. The longitudinal folds may extend into it for a variable distance. It is normally smooth and regular in outline.
4. The portio frequently shows on the plates.

Certain pitfalls have been encountered during the course of our work which may lead to errors in or interfere with the radiologic diagnosis. We have previously warned against the introduction of air. An air bubble can produce a clear rounded shadow similar to a polyp. Attention



Fig. 1.—A, Hystero-gram showing small polyp in the fundus. B, Small fibroid protruding into the fundus resembling a large polyp.

tion has also been called to the necessity of a free return of the excess fluid around the cannula in order to prevent, if possible, the passage of solution through the tubes. We have seen no serious effects from spill into the peritoneal cavity, but confusing shadows are produced by deposit of the material outside of the uterus and tubes which make the plates unsatisfactory for diagnosis. Contrast material in the tubes does not usually interfere with the study. In one case with retrodisplaced uterus, it did cause confusing shadows. The material deposited in this manner remained in the tubes for three weeks. It was our impression that we had demonstrated a hydrosalpinx. Examination of the specimen removed at operation showed this to be an endometriosis of the tubes. The presence of opaque material in the gastrointestinal tract may prevent a satisfactory examination. One such case occurred in which the defect produced by the bulging of a fibroid into the uterine cavity, as



well as an irregularity of the surface immediately below that point, caused by an early carcinoma, were obscured on all but one plate by the presence of a bismuth mixture in the colon. Satisfactory examination of the latter area is quite impossible on this account.

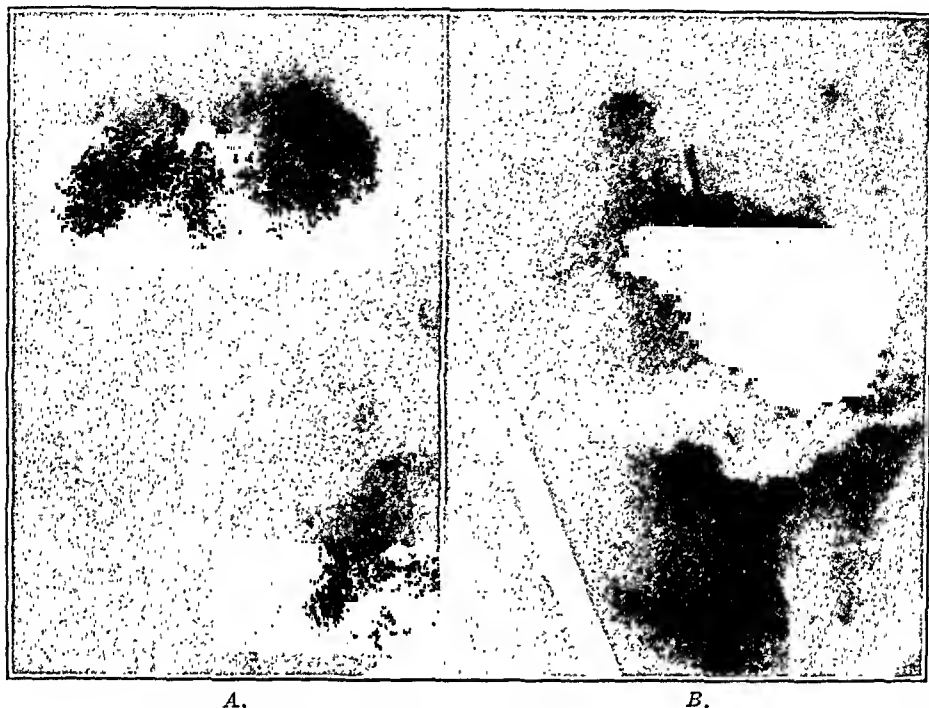


Fig. 2.—A, Hyperplasia. Note regularity of uterine contour. B, Advanced malignancy (adenocarcinoma). Note irregularity of shadow.

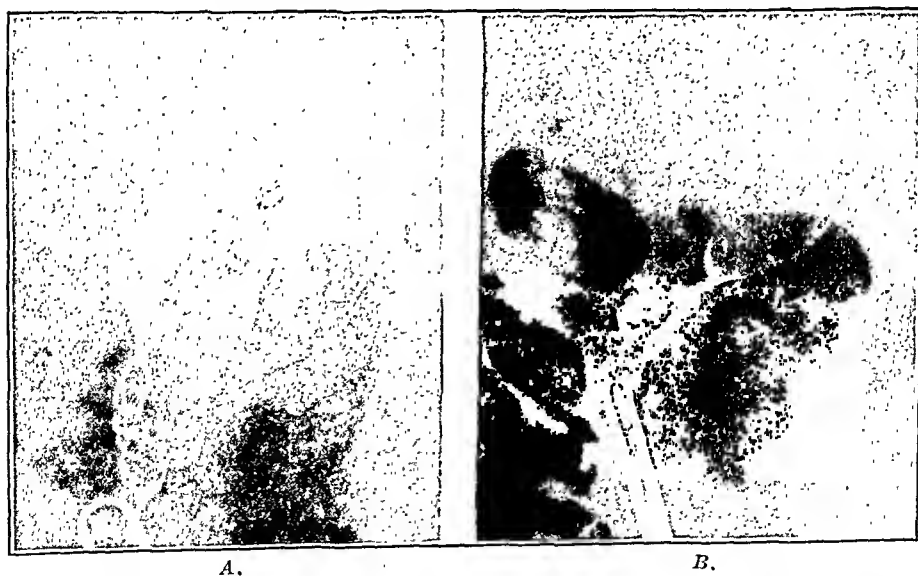


Fig. 3.—A, Uterine fibroid. Examination on account of profuse bleeding. B, Hystero-gram of same case six months following radium treatment. Patient symptom free.

In case of large pelvic tumors we have found the method useful in differentiating between those displacing the uterus and those involving it. The former are characterized by the presence of a uterine shadow

of normal size and shape in an abnormal position. The latter show varying degrees of distortion of the uterine cavity:

The examination of cases in which intrauterine lesions were suspected has yielded much interesting information. Hyperplasia has been diag-



Fig. 4.—A, Malignancy in cornu of uterus (adenocarcinoma). B, Demonstration of radium application; radium tube held in the involved cornu close to the lesion.



Fig. 5.—A, Demonstration of unsuccessful attempt to place one radium tube in each cornu. B, Good application of radium showing tubes in proper position.

nosed by extreme enlargement of the folds without loss of smooth outline. With the broadening of the folds there is a corresponding decrease in their number.

Frequently small polypoid elevations are shown on such films in the form of tiny, smoothly rounded shadows. Larger polyps have been located in other cases. They are characterized by clear circular shadows surrounded by rings of contrast material. If the base of the polyp is broad it may be caught in profile on some of the films.

Small submucous fibroids, if protruding far into the uterine cavity, may produce the same type of shadow. The indentation caused by protrusion of most submucous fibroids is sharply defined and with smooth margins. The endometrium is stretched and shows a few faint markings over the lesion. Larger fibroids show marked deformity of the cavity on the films.

Some cases (of fibroids) have been examined six months after radium treatment. Marked shrinking of the lesion has been shown with decrease in size of the cavity and atrophy of the endometrium. On account of the unusually smooth surface and the diminished production of mucus, very little contrast material will adhere to the surface and the shadows are faint.

Other defects in the shadow of the corpus have been detected. They do not produce the clean-cut margins characteristic of fibroids. Endometrioma has been found and masses of retained products located. In case of small flat lesions, like the former, we feel that radiologic diagnosis alone is not safe and that immediate biopsy is indicated. In the latter instance the ovoid shape of the cavity is the clue to diagnosis.

Carcinoma produces irregularity in the uterine outline. In the cervical canal the early lesion exhibits only a localized narrowing and slight irregularity. Occasionally a small crater can be demonstrated. In more advanced lesions the shadows may be broader, the margins more irregular and deep ulceration shown by flecks of material which have penetrated into the small crevices. The margins of the lesion are frequently elevated.

By defining the local limits of the lesion and its depth of ulceration, we have felt that the quantity and distribution of radium could be more accurately gauged. The proper application of the radium tubes can be accurately demonstrated by injecting immediately before or after radium insertion. The outline of cervix and corpus can be shown, the limits of the local lesion defined, and the relation of the radium tubes to the lesion demonstrated.

In the body of the uterus, carcinoma produces only slight irregularity of outline in its early stages. Crater formation has been shown in the region of the internal os. Advanced lesions produce increasing irregularity with evidence of erosion. Radium application is more difficult without plates for control as the radium might easily be placed far from the lesion in the enlarged fundus. This point is well illustrated by the following case:

Mrs. C. D., aged fifty years, gave a history of irregular bleeding for eighteen months. She had passed the climacteric seven years previously. The hysteroqram showed a large irregular defect of the fundus. Biopsy from this area proved the diagnosis of adenocarcinoma. This patient was a poor operative risk and radium treatment was selected as the method of choice. A 50 mg. tube of radium attached to an empty tube to hold it in position in the fundus was inserted into the uterine cavity and the lower tube fixed to the cervix with a clip. Fortunately it passed into its proper position close to the lesion. Treatment was given in this manner for 600 mg. hours. After a twenty-four-hour rest, two tubes, each containing 50 mg., were fastened to wire applicators and inserted at angles designed to pass one into each cornu. A check of the placement showed both tubes in the same cornu, the second one slightly lower than the first inserted. The second tube, therefore, was removed, the applicator wire bent to a different angle and inserted in proper position. Both were fastened by a lead clip at the cervix. It is easy to understand how the radium might all be placed more than 2 cm. from the lesion in cases similar to this and the greater part of the benefit of treatment lost. This may explain some of the poor results obtained from irradiation of lesions in the fundus.

#### SUMMARY

1. A recent method of hysteroqrphy has been described which permits the demonstration of the surface markings of the endometrium.
2. Findings on investigation of cases of uterine bleeding have been described. The results have been checked by biopsy or by gross and microscopic examination.
3. Some results of irradiation have been shown.
4. A technic for demonstrating the control and accuracy of radium placement has been discussed.

---

Quénu J., and Bécclère, C.: Metrorrhagia in Young Women and Curettage, Bull. Soc. d'Obst. et de Gynéc. 23: 686, 1934.

The authors curetted 30 young women for metrorrhagia. In 21 per cent of the cases as definite causes for the excessive bleeding were discovered: cancer of the body of the uterus, small submucous fibroids, polyps, and dermoid cysts. In 78 per cent of the cases no histologic lesions could be demonstrated. However, in more than half of these cases there existed a chronic infection of the genitalia most likely responsible for the bleeding. In not a single instance did curettement lead to any complication.

A follow-up after seven years showed that five patients had to have further operations because the bleeding returned. Four were operated upon and one was treated by roentgen ray therapy. In five more patients irregular bleeding recurred but apparently no further treatments were given. In two women the profuse bleeding ceased but abdominal pains persisted. Only in seven women did the menstrual periods become regular and normal. Four of these patients subsequently became pregnant. This means that 50 per cent of the patients had recurrences. Therefore, curettement alone is not a satisfactory treatment.

J. P. GREENHILL.

## WHEN IS SURGERY INDICATED IN RETRODISPLACEMENT OF THE UTERUS?

GEORGE H. GARDNER, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology of Northwestern University Medical School and the Gynecological Service of Passavant Memorial Hospital)

THE material for this paper has been accumulated from a review of the histories of 145 women with retrodisplacement on whom Dr. Arthur H. Curtis or I have operated during the past five years. These cases have been gleaned from a large number of women with retrodisplacement and represent the group in whom surgical intervention appeared necessary. However, I have not determined the percentage of retrodisplacements which require surgical correction. In this paper, "retrodisplacement" means *marked* retrodisplacement, usually of a heavy uterus.

### CLASSIFICATION OF CASES

An attempt was first made to determine the importance of the retrodisplacement per se in the production of symptoms; this proved to be a difficult task. In some instances the displacement was obviously responsible for symptoms—these I have termed *essential* displacements; in others it was equally apparent that associated lesions were of chief importance—such cases will be called *incidental* displacements. Many times it was almost impossible to decide whether the uterine displacement or the associated pathology was of greater importance, and the following factors have been considered before classifying these cases either as essential or incidental displacements:

1. Age and social status of the patient
2. Character, time of onset, and severity of symptoms
3. Indications for surgical intervention
4. Type and extent of associated pathology encountered at operation

In 83 (57 per cent), the retrodisplacement seemed to be the essential lesion, and in 62, or 43 per cent, it was apparently only an incidental feature of more important associated pelvic pathology.

### ASSOCIATED PELVIC PATHOLOGY

Practically all, in fact 94 per cent, of these patients presented some associated genital pathology; in only 6 per cent was retrodisplacement the sole abnormal finding at operation. At once a rather pertinent ques-

tion arises: Are the symptoms, from which these women sought relief, due primarily to the displacement or are they caused by associated pathology? In many cases it is certain that the associated genital lesions were of little importance.

Among the 83 which I have termed *essential* retrodisplacements, there were 9 with no associated pathology (but only 1 was nulliparous); 19 presented childbirth injuries which also required surgical correction; 11 had endometriosis; there were 10 with cervicitis and leucorrhea which necessitated cauterization or amputation of the cervix; 8 had residues of pelvic infection; 7 had uterine fibroids; 5 had small ovarian cysts; 5 had painful postoperative adhesions; 5 had appendicitis; 2 had both fibroids and endometriosis; 1 had a fist-sized parovarian cyst; and 1 had a localized adenomyoma of the uterus.

Of the 62 patients with *incidental* displacement, there were 12 with residues of pelvic infection and 11 with symptom-producing childbirth injuries, such as prolapse, procidentia, rectocele, and cystocele; 8 were complicated by extensive pelvic endometriosis; 8 were older women, at the menopause, whose sole complaint was bleeding; 5 had appendicitis and the correction of the displacement was largely a prophylactic measure; 4 were operated upon chiefly to relieve adhesion pain; 4 had childbirth injuries with associated endometriosis; 3 had uterine fibroids; 2 had large ovarian cysts; 2 had both fibroids and endometriosis; 1 had both childbirth injuries and fibroids; 1 had an ectopic pregnancy; and 1 had tuberculous salpingitis.

#### AGE

Most of our patients were young women; their average age was 32.4 years. The average age in the essential displacement group was 30 years; in the incidental series, it was 35.5 years.

#### MARITAL STATUS

There were 20 unmarried women whose average age was twenty-eight years, and 125 married women averaging 33.1 years. Twelve of the unmarried are classified as essential displacements and 8 as incidental; in other words, about 13 per cent of each group were unmarried nulliparous women and 87 per cent were married.

#### SYMPTOMS

The most frequent symptoms were (1) lower abdominal discomfort, (2) uterine bleeding, (3) dysmenorrhea, (4) sterility, and (5) backache.

1. *Lower Abdominal Discomfort*.—A bearing-down sensation, with a feeling of weight and heaviness in the lower abdomen and pelvis, occurred in 68, or 47 per cent, of the patients. Forty-four (30 per cent) suffered from an almost constant

lower abdominal ache, often exaggerated during menstruation. In 18 there was no complaint of abdominal pain; in 10, it was definitely appendix distress and in 5, the pain resulted from postoperative adhesions.

2. *Uterine Bleeding*.—Ninety-four, or 65 per cent, of the patients had abnormal uterine bleeding, and in 51 there was no deviation from the normal.

In 25 patients the periods were prolonged and profuse; in 23 the loss of blood was excessive; 15 menstruated too frequently, flowed too long and bled excessively; in 8 the periods were prolonged (ten days or longer); in 8, bleeding occurred too frequently, every week or two; in 8, there had been continuous uterine bleeding for weeks; and in 7 there was intermenstrual spotting which sometimes tended to appear about the middle of the menstrual cycle.

Of the 51 women who gave histories of normal menstruation, 29 are classified as essential displacements and 22 as incidental. In other words, 35 per cent of each group menstruated normally although bleeding was one of the indications for operation in 65 per cent of the patients.

3. *Dysmenorrhea*.—In 63 patients (44 per cent), there was insufficient menstrual pain to call it a complaint; 37 (26 per cent) had acquired dysmenorrhea during adult life; 29 had always had crampy discomfort; 14 complained of a bearing-down discomfort; and in 2 the chief discomfort was pain in the appendix region.

Of the 37 complaints of *acquired* dysmenorrhea, 16 occurred in essential displacements and 21 in the incidental group. In other words, 19 per cent of the essential cases acquired an intense dysmenorrhea during adult life, while it appeared in 34 per cent of the incidental displacements. There were 14 cases each, of essential and incidental displacement, who showed endometriosis and adenomyosis. Five of the 14 essentials, or 36 per cent, complained of acquired dysmenorrhea, but it occurred in 11 or 79 per cent of the incidental displacements with endometriosis, again emphasizing the importance of acquired dysmenorrhea as a symptom of pelvic endometriosis.

4. *Sterility*.—Among the 19 married women who complained of sterility, 9 had extensive pelvic endometriosis; in 3, it was found that the tubes had been removed at a previous operation; 2 had uterine fibroids; 1, the residues of a gonorrheal infection with occluded tubes; 1, the residues of a postabortive infection with phimosis of the fimbriated ends of the tubes; another, tuberculous salpingitis; in another, the ovaries were unusually large, cystic and edematous, a three-inch, right-sided, parovarian cyst was present, the cervix was inflamed and was the source of an annoying leucorrhea; in another, the only associated pathology was a three-inch corpus luteum hematoma. Retrodisplacement, per se, was not responsible for the sterility of these women.

5. *Backache*.—Eighty-one (56 per cent) patients did not complain of backache; in 19 the character and site of the pain was not described; in 18 or 12 per cent it was said to be in the low back, often a dragging ache accentuated at menstrual times and in some instances relieved by wearing a pessary; in 17 the ache was located in the lumbar region; 5 patients were known arthritics; and in 5 there was sacroiliac disease. Consequently the retrodisplacement could not have been responsible for backache in more than one-fourth of our patients.

It is usually possible to differentiate an orthopedic backache from one of genital origin. This is best accomplished by a carefully elicited history and a complete physical examination with accurate localization of the site of the pain, also through attempts to reproduce or accentuate the backache by making traction on the uterus, especially on the uterosacral ligaments, or to relieve it with an appropriate pessary. Such procedures permit the examiner to predict before

operation whether relief from the backache will follow correction of obvious genital pathology. *Not a single patient was operated upon solely for the relief of backache.*

6. *Miscarriages.*—Seventy-six or 61 per cent of the married women had had no miscarriages and 34 or 27 per cent had had 53 spontaneous miscarriages. However, there had been 238 full-term pregnancies, consequently the incidence of spontaneous miscarriage was only 18 per cent; for the state of Illinois it is estimated to be 20 per cent. *None of the patients of this series came to operation because of a tendency to abort repeatedly.*

#### INDICATIONS FOR SURGICAL INTERVENTION

The four chief complaints, viz., lower abdominal discomfort, bleeding, dysmenorrhea, and sterility, were grouped as symptoms and constituted the indications for operation as follows:

1. Lower abdominal discomfort, dysmenorrhea and bleeding	43 cases
2. Lower abdominal discomfort and bleeding	27 cases
3. Lower abdominal discomfort and dysmenorrhea	21 cases
4. Lower abdominal discomfort	21 cases
5. Bleeding	8 cases
6. Lower abdominal discomfort, dysmenorrhea, bleeding and sterility	7 cases
7. Bleeding and dysmenorrhea	6 cases
8. Lower abdominal discomfort, dysmenorrhea and sterility	4 cases
9. Sterility	3 cases
10. Lower abdominal discomfort, bleeding, and sterility	2 cases
11. Lower abdominal discomfort and sterility	2 cases
12. Dysmenorrhea, bleeding, and sterility	1 case

#### OPERATIVE PROCEDURES

*Types.*—The operations have been divided, according to the manner of approaching the uterus, into 124 *abdominal* and 21 *vaginal* procedures. Preservation or forfeiting of the childbearing function has permitted a further division into *reconstructive* and *destructive* operations, respectively.

*Abdominal Reconstructive Operations.*—The classical abdominal replacement operation which we have employed most frequently utilizes all supporting structures in maintaining the uterus in an anterior position; at the same time it preserves the normal mobility of the uterus. This operation consists of three separate steps: First, suturing together the relaxed uterosacral ligaments with silk for a distance of  $1\frac{1}{2}$  to  $2\frac{1}{2}$  inches below their cervical insertion in conjunction with silk suturing of the lax posterior leaves of the broad ligaments to each other and to the uterus, often to a rather high point on the posterior surface of the uterus. Second, a Baldy-Webster round ligament operation, performed with silk. Third, advancement of the bladder reflexion from its almost invariably low level on the cervix to a more nearly normal location on the fundus.

Such a replacement operation builds a basement of support for the uterus from the uterosacra and posterior leaves of the broad ligaments. The Baldy-Webster technic is not only of great value in maintaining an anterior position



of the uterus but also tends to correct the commonly associated prolapse of the ovaries. Sometimes the uteroovarian ligaments are still so attenuated that further shortening is necessary; this is accomplished by angleworm reefing with silk. Advancement of the reflexion of the bladder is important in keeping the uterus forward. When a tube or a tube and ovary have to be removed, or if the round ligaments are not markedly attenuated, we sometimes substitute an *angleworm reefing of the round ligaments*, with silk, for the preferred Baldy-Webster technic.

Sixty-nine patients (48 per cent) were subjected to reconstructive replacement operations; 47 were classical replacements and 22 included reefing of the round ligaments.

*Destructive Abdominal Operations.*—Defundation, with suturing of the uterosacrals and posterior leaves of the broad ligaments together with advancement of the bladder, has been employed when further pregnancies were impossible or inadvisable, and a preservation of regular menstruation was desired. Removal of the fundus was resorted to fifteen times.

Thirty-two patients were subjected to supravaginal and eight to complete hysterectomy. The uterosacral ligaments were frequently sutured together and to the cervix after a supravaginal hysterectomy.

Many of the patients in these abdominal cases were also operated upon vaginally, for repair of a cystocele, lacerated perineum and rectocele, or an unhealthy cervix. If the vaginal work includes correction of a cystocele, the usual advancement of the bladder reflexion within the abdomen is omitted not only because it is unnecessary but it also may increase the incidence of infection.

*Vaginal Operations.*—Vaginal operations alone were performed twenty-one times but only for *incidental* displacement of the uterus. Extensive plastic procedures were necessary for most of these cases. There were 9 vaginal hysterectomies; 6 patients were curetted for diagnosis and the menopause was induced in 5 with radium and in one with x-ray; in 5 the Watkins' interposition operation was the procedure of choice (twice after vaginal defundation); and in only one did the technic include transfer of the bases of the broad ligaments.

## RESULTS

One hundred twenty-one patients (85 per cent) have obtained complete symptomatic relief and an excellent clinical result; 4 have failed to report for examination; and 2 died, both from pulmonary embolism. Seven have slight sagging of the uterus, 2 of these followed subsequent deliveries, *but in not a single patient has the uterus returned to a retro-displaced position*. Four have small cystic adnexal tumor masses which cause moderate discomfort; 3 of these occurred in patients with residues of pelvic infection; 1 followed a supravaginal hysterectomy; and 2 occurred after defundation attended by a febrile convalescence. Two patients with endometriosis, subjected to a conservative reconstruction type of operation, continue to have marked dysmenorrhea and some bleeding; 2, with pelvic residues, developed postoperative cystic tumor masses and had to be reoperated. One patient has residual thrombophlebitis although the pelvic symptoms, for which she was operated,

have been completely relieved; another complains of pelvic pain, apparently the result of postoperative adhesions which followed a previous operation; one continues to menstruate twice a month but the uterus is in excellent position.

Nineteen patients complained of sterility but 3 were found to have had the tubes removed at a previous operation. In 7 it was necessary to perform a destructive type of operation, not compatible with subsequent conception. Nine reconstructive operations were attempted and 2 of these patients have subsequently been delivered of healthy babies.

Eleven women became pregnant following replacement operations, but we have had an opportunity, thus far, to examine only 3 of these patients after delivery; one has a perfect anatomic result, in the other two there is a slight tendency to sagging of the uterus (both were reefing cases). However, obstetricians tell me that the classical abdominal replacement operation which we advocate does not interfere with the normal progress of labor and the uterus returns to its anterior position following delivery.

*Additional Data.*—In six patients an acutely inflamed appendix was found at operation; in only 2 was there a preoperative diagnosis of *acute appendicitis*; the others were unsuspected findings.

*Adhesions of the anterior surface of the liver* were found six times. Massive adhesions were encountered in the patient with tuberculous salpingitis. Five, with gonorrheal tubal disease, had typical adhesion bands of the anterior surface of the liver. Such adhesions, as described by Dr. Curtis, are found so frequently in patients with gonorrheal tubal disease that we consider their presence almost pathognomonic of a preexistent gonorrheal pelvic infection.

Of 17 patients subjected to *defundation*, 15 were operated upon by the abdominal route and 2 vaginally; 1 of the vaginal cases developed a large pelvic abscess which was drained. Only 7 of the abdominal defundations pursued a normal postoperative course; 5 were febrile; 1 had a pulmonary embolus and 2 developed infected wounds.

Of 22 patients in whom replacement of the uterus included a *reefing of the round ligaments*, 16 are known to have obtained a good result; 1 failed to report for examination; in 5 (23 per cent) there is some sagging of the uterus.

Only 4 patients with retroflexion had had the *cervix cauterized* prior to their abdominal operation. In 2 there was no history of pelvic infection and no evidence of it was found at operation; in the other 2, however, adhesions and scar tissue encountered at operation confirmed our impression that endocervical cauterization of a markedly retrodisplaced uterus is inadvisable.

Five women with retrodisplacement and menopausal bleeding were subjected to diagnostic curettage and intrauterine radiation (1200 to 2000 mc.); none of this group developed pelvic infection.

#### CONCLUSIONS

1. Retrodisplacement of the uterus per se may be responsible for lower abdominal and pelvic discomfort, uterine bleeding and dysmenorrhea; these symptoms are amenable to relief by operative intervention.

2. The findings at operation indicate that retrodisplacement of the uterus is a menace to the health of the ovaries and is responsible for the development of large, edematous, cystic ovaries which function abnormally; and equally important, retrodisplacement apparently predisposes to endometriosis and perhaps to uterine fibroids.

3. The operative replacement of a symptomless, large, heavy, dragging retroflexed uterus, in younger women, is *sometimes* a justifiable procedure as a prophylactic measure.

4. In this series retrodisplacement was an infrequent cause of backache; it alone was not responsible for sterility and apparently did not increase, materially, the incidence of spontaneous abortions.

5. The surgical correction of retrodisplacement should embrace a utilization of all supporting structures, namely the uterosacral ligaments, the posterior leaves of the broad ligaments, the round ligaments, and the peritoneal reflexion of the bladder.

6. A recurrence of the retrodisplacement has not occurred in this series after subsequent pregnancies nor has there been any interference with the normal progress of labor.

7. Substitution, in selected cases, of an angleworm reefing of the round ligaments for the Baldy-Webster technic is helpful, but it is not an ideal procedure.

8. Defundation, employed in the cure of retrodisplacement, is followed by postoperative complications more frequently than is supravaginal hysterectomy.

104 SOUTH MICHIGAN AVENUE

---

NOTE.—Four other papers presented at this meeting, those of Drs. Healy, Bonney, Caldwell, and J. M. Hundley, Jr., will be included in the November issue, together with the first installment of the discussions.

# Department of Reviews and Abstracts

---

CONDUCTED BY HUGO EHRENFEST, M.D.

---

## Selected Abstracts

### Radiography and Radiotherapy

Heyrowsky, K.: When Is an X-Ray Picture Indicated in Obstetrics? *Med. Klin.* 30: 1630, 1934.

Obstetricians should resort to x-ray to clear up any indefinite situation. When complications are due to pelvic contraction an x-ray picture will indicate whether or not a patient should be delivered in a hospital or at home. The x-ray will demonstrate anomalies in the shape of the pelvis. The author emphasizes that clinical measurements are by no means as reliable as the measurements obtained by means of x-ray plates. X-ray pictures of lateral views are most helpful and are absolutely indicated in all cases of contracted pelvis, funnel pelvis, and spondylolisthesis. In cases of abnormal presentation and deflection attitude, a correct diagnosis can easily be made by means of x-ray pictures. Furthermore, the x-ray will verify a diagnosis of multiple pregnancy, monsters and a suspicion of intrauterine death of the fetus.

The author does not believe in the use of x-ray pictures for the purpose of measuring the fetal head, because thus far none of the methods advocated for this purpose have proved practical. He emphasizes particularly that chief reliance in obstetric difficulties should be placed upon clinical examination, and that x-ray pictures should be the last resort. In the vast majority of cases labor may be conducted safely without x-ray pictures. Exposures for x-ray pictures have absolutely no harmful effect upon the baby.

J. P. GREENHILL.

Wahl, F. A.: Roentgenology in Obstetrics, *Arch. f. Gynäk.* 152: 173, 1933.

Roentgenology provides valuable assistance in obstetrics in those instances in which physical and clinical examinations do not reveal all of the necessary information. Many cases which are obscure from a diagnostic point of view are cleared up by roentgenographic studies. The location and position of the fetus, station of the presenting part, and the relationship between head and pelvis and multiple pregnancies are clearly shown on x-ray plates. It is the most accurate method of determining malformation or death in utero. It should never be omitted as a safeguard before cesarean section. At times a single plate will not give all the necessary data but the author warns against repeated films on account of possible danger to the fetus.

RALPH A. REIS.

Hajkis, Miron: Radiographic Evidence of Live Birth, *Lancet* 2: 134, 1934.

The author states that the radiographic evidence of air in the lungs and the duodenum is strong proof of live birth. Air may be blown into the stomach by mouth-to-mouth breathing but not into the duodenum. He also remarks that the lungs of stillborn infants could not be inflated artificially.

Atelectasis is most pronounced in the bases of the lungs, and more in the left than the right.

This procedure is of medicolegal import, even realizing that putrefaction may produce gas but this will be as bubbles and not as air-filled alveoli or bowel.

H. CLOSE HESSELTINE.

Béclère, C.: Metrorrhagia Among Young Women, *Bull. Soc. d'obst. et de gynéc.* p. 688, 1934.

Béclère has observed 70 cases of metrorrhagia in young women where the etiology was unknown. In such cases he has employed hysterosalpingography and believes this to be the best means of exploration of the uterus. It is simple, rapid, and without danger. It is the only means of detecting a beginning cystic salpingitis. It likewise reveals intrauterine lesions such as retention of placental tissue, polyps, submucous fibroids, and cancer of the body of the uterus. It also gives information concerning lesions of the tubes. If hystero-graphy is performed systematically it will permit limitation of curettement to those cases where there exists an intrauterine lesion. Curettement will then be necessary in only one-eighth of all cases of metrorrhagia in young women. The author points out that chronic infection of the genitalia is a frequent cause of bleeding because he found infection in two-thirds of his cases. Hence, treatment should be directed against infection. Patients with cystic salpingitis should be operated upon and the others treated by means of vaccines and medical diathermy.

J. P. GREENHILL.

Jarcho, J.: The Value of the Roentgen Ray in Gynecology, *Am. J. Surg.* 21: 13, 1933.

Uteros-alpingography is of the utmost importance: (1) in establishing the patency or nonpatency of fallopian tubes and definitely locating the site of blockage in cases of occlusion; (2) in restoring the patency of occluded tubes; (3) in suggesting the best site for a stoma in operations on sealed tubes or indicating the part of the tube to be resected; (4) in determining the success of salpingostomy and preventing the stoma from contracting and closing secondarily; (5) in the diagnosis, prognosis, and treatment of chronically inflamed and occluded tubes; (6) in deciding in cases of fibroid of the uterus upon the most advisable therapeutic procedure, whether surgical interference, roentgen, or radium treatment; (7) in making a differential diagnosis, in settling differences of opinion in pelvic diagnosis, and in providing a permanent record for future use.

J. THORNWELL WITHERSPOON.

Béclère, C.: Accidental Vascular Injection in the Course of Hysterosalpingography, *Bull. Soc. d'obst. et de gynéc.* p. 31, 1933.

In 1926 Béclère published two reprints of roentgen ray pictures which demonstrated the injection of iodized oil into blood vessels during experimental work. At that time he cautioned against the use of excessive pressure in the instillation of lipiodol. In 1929 Brull, Vaurell and Riera demonstrated the accidental injection of

lipiodol into blood vessels in a woman. (Since then other reports of this accident have appeared, J. P. G.) Bécélère says that he has not infrequently detected such accidents in the published pictures of other authors who did not recognize the complication and assumed the shadows indicated tubal permeability. Hence this accident is more common than is generally believed.

Vascular injection of lipiodol can occur only if both tubes are obstructed. The day after the injection, the iodized oil has escaped into the general circulation and cannot be found in the pelvis.

The accident occurs (1) when too much pressure is exerted in the presence of closed tubes, (2) when the uterine cavity is very small in cases of underdevelopment and the tubes are sealed off, and (3) where salpingectomy has been performed and there are abnormal vascular anastomoses. On the other hand, it is rare in cases of metrorrhagia. Fortunately accidental injection of lipiodol is well tolerated by the patient.

J. P. GREENHILL.

Shute, E., and Davis, M. E.: *Histologic Changes in Rabbits and in Dogs Following the Intravenous Injection of Thorium Preparations*, Arch. Path. 15: 27, 1933.

By means of intravenous injection of colloidal preparations of thorium, viz: tordiol, umbrathor and the less toxic thorotrast, Shute and Davis were able to secure visualization of the liver and spleen in rabbits and dogs but were unable to visualize the placenta. These authors used smaller doses than did others for successful placental visualization in the rat. Even their smaller dosages produced intense degeneration of the liver and spleen and caused one rabbit to abort and to have a spontaneous rupture of the spleen and a postpartum hemorrhage. They state that colloidal thorium has no place in clinical work.

Particles of thorotrast practically disappear from the liver and spleen in two or three months after injection, and the cells regain an almost normal appearance. The placenta of the dog and of the rabbit appears to be an effective barrier to the transmission of thorium to the fetus. With the exception of the animal mentioned, all of their pregnant animals carried their young to term or were killed near term for study. The metal could be found in the rabbit placenta microscopically up to eleven days after injection, but by this time it was in the form of very fine particles and after that seemed to disappear. Placental cells do not show the destructive changes observed in the cells of the liver and spleen.

W. B. SERBIN.

Gilbert, P.: *Radiotherapy of Tuberculous Adnexitis*, Bull. Soc. d'obst. et de gynec. p. 606, 1933.

The tubes are involved in 80 to 90 per cent of all cases of tuberculosis of the female genital tract. The diagnosis is difficult to make before operation and even at operation it is impossible to recognize the true diagnosis in most cases. Microscopic examination is necessary.

The indications for radiotherapy in this condition depend upon the age of the patient and the severity of the lesions. In young women radiotherapy should be used only if change of climate, heliotherapy and ultraviolet rays have failed. Even in apparently hopeless cases, radiotherapy should be tried. The action of the roentgen rays is not directly on the tubercle bacilli but upon the tubercles which are radiosensitive. In serious cases, all ovarian function should be eliminated.

Gilbert treated 13 women who had tuberculous salpingitis with roentgen rays. In 9 cases there was a clinical cure, in 5 cases there was considerable amelioration and 3 women died of a continuation of the tuberculous process.

J. P. GREENHILL.

Jacobi, H., and Lindner, J.: Indications, Results and Failures of Roentgen Ray Castration, *Monatsh. f. Geburtsh. u. Gynäk.* 94: 178, 1933.

From 1928 to 1931 roentgen rays were used for the purpose of producing castration in 383 women. Twelve women could not be traced and 4 died. Among the 367 remaining women, there was an amenorrhea after one or more bleedings in 96.2 per cent of all the cases. If the roentgen rays are applied to the ovaries in the first half of the menstrual cycle, amenorrhea sets in more quickly than if the rays are applied in the second half of the period. Likewise the older the patient, the more quickly will amenorrhea result after radiation. In 14 women (3.8 per cent) an amenorrhea failed to result.

No harmful sequelae were observed after radiation. Forty-one women complained of hot flashes and 35 had palpitation, headaches, and abdominal discomfort.

J. P. GREENHILL.

Tesauero, G.: Pregnancy After X-Ray Treatment of the Mother, *Ztschr. f. Geburtsh. u. Gynäk.* 102: 522, 1933.

In a series of 68 patients who were subjected to ovarian-stimulating doses of x-ray for various reasons, mainly for amenorrhea and oligomenorrhea, 18 subsequently became pregnant and delivered 21 children. In 5 cases pregnancy occurred within the first year after treatment, in the remaining ones in from one to six years. The x-ray dose was never over 10 per cent of the erythema dose, ranging mainly from 2 to 5 per cent.

All pregnancies and all deliveries ran a normal course. The children were observed over a period of five years. No anomalies of growth or general development were noted. The writer merely states these facts, considering the number of cases too small to warrant conclusions.

GROVER LIESE.

Husted, E.: On X-Ray Treatment in Certain Forms of Metrorrhagia, *Acta obst. et gynec. Scandinav.* 13: 103, 1933.

Hypertrophica irregularis glandularis endometrii is found chiefly in women near the climacterium, but occurs also in young and relatively young women. It seldom occurs during the menopause.

The endometrial changes are associated with quite irregular, often protracted or profuse hemorrhages which may lead to a marked degree of anemia; in several cases the abnormal hemorrhage is preceded by an interval considerably longer than that of the normal menstrual cycle.

Physical examination of the patient usually reveals no definite abnormality other than some degree of anemia; nor does gynecologic examination as a rule show any abnormality. An abnormal condition of the adnexa is made out only in a very few cases. Hence the diagnosis can be made only by histologic examination of the endometrium, by demonstration of the typical changes. The endometrial changes are very likely to recur after curettage.

X-ray treatment has given excellent results; it has been easy to carry out, and ambulatory treatment was given without any inconvenience in the great majority of the cases reported by Husted. Among 100 patients treated with x-rays who were

examined one to eight years after the treatment, only two had a relapse. In one of these, the condition proved refractory to x-ray treatment requiring operation.

In most of the patients the x-ray treatment was followed by symptoms of ovarian insufficiency, usually of a fairly mild character, giving actual discomfort only in about one-fourth of the cases. These symptoms, on the whole, appear to have been no worse than the average run of such complaints in connection with the normal climacterium.

The conclusions that may be drawn from the material presented as to the treatment of those cases of metrorrhagia in which there is irregular glandular hypertrophy of the endometrium are as follows:

In older patients, near the climacterium, x-ray treatment is indicated when the diagnosis is established by the histologic findings.

In younger patients, in the latter part of the thirties, without beginning symptoms of ovarian insufficiency, the effect of curettage is awaited; if there is a relapse of the condition, x-ray treatment is given, after repeated curettage when required.

Hysterectomy ought to be the ultimate resort to fall back upon only in the extremely rare instances where the hemorrhages cannot be checked by x-ray treatment.

J. P. GREENHILL.

Vogt, E.: *The Roentgen Ray and Radium Treatment of Inoperable Ovarian Carcinoma*, Med. Klin. 29: 1464, 1933.

The experience of Vogt with the postoperative roentgen ray and radium treatment of inoperable carcinoma of the ovary leads him to conclude that in cases of operable carcinoma of the ovary it is wise to employ postoperative roentgen ray treatment prophylactically. A full dose is administered. In cases of inoperable cancer of the ovary where the diagnosis was proved by exploratory laparotomy and biopsy, the author combines a full roentgen ray dose with 2,000 mgm. hours of intrauterine radium. This is repeated two or three times. Vogt believes that combined roentgen ray and radium therapy gives better results than roentgen ray treatment alone.

J. P. GREENHILL.

Nielsen, M.: *Radium Treatment of Cancer of the Cervix During Pregnancy*, Acta obst. de gynec. Scandinav. 13: 235, 1934.

Cancer of the cervix is a rare complication in pregnancy (about 0.005 per cent). Whether cancer of the cervix takes a particularly rapid course during pregnancy is a question that cannot be answered generally, but it is a striking fact that the cancer is often inoperable in the latter half of the gestation period when the patient applies for treatment. A report is given of 3 cases of postconceptional radium-treated cancer of the cervix, together with a review of 41 cases gathered from the literature.

In 12 out of these 44 cases the pregnancy was interrupted by abortion. Among the 32 children who were born at term or nearly so, only 3 were defective as a result of the treatment. Thus the prognosis is relatively good as far as the children are concerned. For the mothers the prognosis is poor, only 8 being alive three years after the treatment. Labor at term or abortion was spontaneous in 32 of these patients; 5 of these died from hemorrhage during parturition, 2 from infection. Operation was performed in 12 cases: Cesarean section in 5 (one with fatal outcome, eclampsia), cesarean section with supravaginal amputation of the uterus in 4 (one died), and cesarean section with total hysterectomy in 4 (all fatal).



Out of regard for the child the author advises against intracervical radium treatment, and, on account of the danger of fatal hemorrhage during parturition at term, cesarean section is recommended, with supravaginal amputation if advisable.

J. P. GREENHILL.

Porcaro, Diego: *Bullettino della Sacreta Piemontese*, Arch. di ostet. e ginec. 40: 295, 1933.

The author reports his results with x-ray treatment of the pituitary and thyroid glands in women suffering from surgical menopause. The study is based on 11 cases, in which excellent results were obtained in 9. The results on 2 women were negative. The x-ray dose on both the pituitary and thyroid glands was a stimulating one. The blood pressure and pulse rate were recorded. Following the treatment the blood pressure was lowered and the pulse rate slower.

AUGUST F. DARO.

---

## Items

### American Board of Obstetrics and Gynecology Examination

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, December 7, 1935.

Application blanks and booklet of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for this examination must be filed in this office not later than November 1, 1935.

---

The *Editors* are pleased to announce the resumption in an early issue of the discussions of papers read at the meetings of the various societies of which this JOURNAL is the official organ. It is necessary, in order to conserve space, to condense this material as much as possible, but it is hoped that as published, the discussions will add much to the value of the papers.

---

### Erratum

In the article by Drs. Allen and Reynolds in the September issue of the JOURNAL, on page 318, the fifth and sixth lines under "Note" should read: In this paper the B-type crystals of progestin (m.p. 128°) are known now as A *progesterone*, and the C-type crystals of progestin (m.p. 120.5°-121°) are now known as B *progesterone*.

UNIVERSITY OF WASHINGTON  
SCHOOL OF NURSING  
HARBORVIEW DIVISION.



BARTON COOKE HIRST 1861—1935

# American Journal of Obstetrics and Gynecology

---

VOL. 30

ST. LOUIS, NOVEMBER, 1935

No. 5

---

## IN MEMORIAM

### Barton Cooke Hirst

BARTON COOKE HIRST died September 2, 1935, at his home in Philadelphia, of acute dilatation of the heart. He was born in Chestnut Hill, Philadelphia, on July 20, 1861, the son of William Lucas Hirst, a prominent attorney, and Lydia Barton Cooke. The Hirst family tree is traced in England as far back as the twelfth century, and the American branch of the family springs from John Hirst, who emigrated and settled in Bethlehem, Pennsylvania, in 1749. The tradition of the family was the law, there having been generations of Dr. Hirst's forebears in Temple Bar, London, and his decision to study medicine was an early evidence of the independence of thought which was always a salient characteristic.

Dr. Hirst married Elizabeth Haskins Dupuy Graham of Philadelphia in 1890, who survives him, as do also a daughter, Mrs. Elizabeth Dupuy Graham Lippincott, and two sons. Barton, Junior, an aviator in the late War, and Dr. John Cooke Hirst 2nd, an obstetrician of Philadelphia. The third son, Thomas, a First Lieutenant in the 151st Field Artillery, died in action in the late War.

Dr. Hirst entered the College Department of the University of Pennsylvania from the Faires Academy with the class of 1882, but at the end of his freshman year, having made up his mind as to his life work, another example of his independence and early maturity, he entered the Medical School, graduating with the class of 1883. Subsequent to his graduation in medicine he served as an interne in the University Hospital and then studied in Heidelberg, Vienna, Berlin, and Munich, where he became an interne with *teaching* duties. This Munich appointment probably had a great deal to do with his lifelong fight for better teaching in obstetrics. At the time of this appointment, eighteen months after his graduation, from the highest type medical school in the United States, he personally had never confined a woman, while on the other hand many of the students whom he had to teach and direct had made deliveries in more than one case. It goes without saying that a man of his mental attributes could not but make an odious comparison between the teaching abroad and that in

the United States. In any event, we know that the practical training in obstetrics for students became one of the ruling passions of his life. When he returned to Philadelphia and was made an assistant to Dr. R. A. F. Penrose, then Professor of Obstetrics at the University of Pennsylvania, there was not a bed devoted to this branch of medicine in the hospital and no arrangements for extramural student obstetrics. As soon, however, as he was elected to succeed Dr. Penrose in the professorship, he filled both of these needs by establishing a maternity department in the hospital and by creating an extramural service for home deliveries by senior students under close supervision. This latter service was and is known as the Southeastern Dispensary. Until Dr. Hirst's retirement from the Undergraduate School he remained largely responsible for its financial support.

At the time of his election to the chair of obstetrics at the University in 1889 the medical faculty was probably the most famous in the history of the school. Agnew, Wood, Pepper, Piersol, Reichert, Norris, Leidy, Wormley, Goodell, Tyson, and White, form a company which might well have given pause to a new member whose life span at that time was twenty-nine years. That he was impressed, goes without saying, but by his sheer professional ability and his ever present tact he was able to make himself acceptable to all of them—no mean feat. It is noteworthy that Dr. Hirst was only the fifth man to hold this chair since the first incumbent, Dr. James, was elected in 1810, the others having been Dr. Dewees, who held it for only one year, and Drs. Hodge and Penrose. It may be said that four men—James, Hodge, Penrose, and Hirst—have divided the occupancy of this chair for one hundred and seventeen years. Dr. Hirst occupied the chair of obstetrics in the University for thirty-eight years, delivering three lectures, or their equivalent, each week to crowded benches, and also personally conducting the large clinical service which he attracted to his ever growing department. The funds needed for new buildings were obtained to a large extent by his personal solicitation.

Dr. Hirst did a vast amount of gynecology as well as obstetrics in his service. He believed, taught, and fought for the interdependence of obstetrics and gynecology, at that time not generally conceded. In this movement he was a pioneer. He felt most strongly that no man unless a skilled pelvic surgeon could be considered a safe obstetrician, and that the reverse was also true, an opinion now almost axiomatic in the minds of those competent to judge, but at that time a very heterodox opinion in most quarters.

When he retired on age in 1927 from the chair of obstetrics in the Undergraduate School he was by far the oldest member of the faculty in point of service. The trustees of the University who in 1907 had conferred upon him the B.A. degree as of the class of 1882, and who subsequently gave him the honorary Doctor of Science degree, elected him, on his retirement from the chair of obstetrics, emeritus professor of obstetrics in the Undergraduate School, and on the amalgamation

of the Howard Hospital with the Graduate School of Medicine of the University, they elected him as professor of obstetrics in that institution with a service in the Graduate Hospital. He held this position until his death, conducting a very active teaching and operative service with the enthusiasm that was his in 1889, and with the ability and knowledge that his ripe experience had brought to full fruition.

Dr. Hirst held many and various positions in the medical world. He was proud to have been the Chairman of the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, and also to have been one of the founders of the American College of Surgeons. He was an enthusiastic member of the American Gynecological Society and one of its former presidents. He was a Fellow of the College of Physicians of Philadelphia since 1888. He was the only member of the Philadelphia Obstetrical Society ever to be elected three times as its president. He was a corresponding member of the Society of Obstetrics and Gynecology of Paris; Consulting Surgeon of the Paris Society of Foreign Surgeons; an honorary member of the Obstetrical Society of Edinburgh and also of the Belgian Gynecological and Obstetrical Society. The University of Pittsburgh gave him the honorary LL.D. degree.

His hospital activities in Philadelphia, aside from the University Hospital and the Hospital of the Graduate School of Medicine comprised staff membership formerly at the Philadelphia General and the Howard Hospital, and latterly until his death he was active on the staff of the Orthopedic and the Lying-In Hospitals. The writer always felt that his first and greatest love was to the Howard Hospital in which for many years he was the mainspring. In fact from the time of his election to the Howard Hospital until its amalgamation with the Graduate School of Medicine of the University it is no exaggeration to say that he was the most active member of its staff. It is a pleasure to bear witness to the fact that after the Howard Hospital had become an integral part of the Graduate Hospital Dr. Hirst transferred his allegiance to that institution.

In his earlier years he was a prolific writer. The *American System of Obstetrics*, edited by him, his *Atlas of Gynecology, Human Monstrosities*, as co-editor with Piersol, and his own two textbooks, the one on *Obstetrics* and the other on *Diseases of Women*, bear ample witness to this fact, not to mention his many scattered articles and papers.

Such is the imperfect record of his achievement, and truly it is an enviable one, but to the many who knew and revered him, it portrays but the shadow of the man himself. The writer had peculiar opportunities to appraise Dr. Hirst at his true value—first as his student, some years later as an assistant on his staff, and a quiz master under him, and for the past eight years as his colleague in the Graduate School of Medicine, and the attributes which have indelibly impressed

themselves were his modesty, his courtesy, his kindliness, which was unfailing, his interest in young men, his enthusiasm for the newer developments in medicine, his keen sense of humor, which made him enjoy a joke on himself at least as much as when another was the subject, an unusual trait, and his marvelous vitality, both physical and mental. Even during the past summer he followed his usual custom with regard to swimming, golf, and sailing; he continued to operate to the end of his life, and within two weeks of his death devised a new technic for sterilization.

As a consultant he was without a peer, not only in his knowledge but in his manifest sympathy with the patient and his meticulous courtesy to the physician. He was an omnivorous reader and a great sufferer from insomnia; this combination resulted in his being thoroughly conversant with general literature, and his interest in art and music must be emphasized. He was the life of the five o'clock social gatherings of medical men in the old days at the University Club before his particular *bête noire*, prohibition, put an end to them. In medical societies he was a most delightful essayist and his discussions of the papers of other men were always courteous, but he never hesitated to be critical when criticism was indicated.

He was a great teacher in the fullest meaning of that term, and in the opinion of thousands of undergraduate students of his day he was by far the best lecturer in the faculty. When it is remembered that actually several thousand men sat under him during his thirty-eight years of teaching, and that what he taught them has been utilized in their daily work among countless women patients, it must be felt that this alone would have been an enduring monument to his memory, even had he done no other meritorious work as a medical pioneer in obstetrical teaching and as a writer.

In his death, premature for him even at his age, medicine has lost an outstanding figure; obstetrics has lost one of the last of the pioneers, and his many friends and colleagues have an abiding sense of a loss which can only increase as time passes.

William R. Nicholson.

---

The Editors of the JOURNAL desire to add to the foregoing memorial an expression of their own sense of personal loss in the death of Dr. Hirst. He was a member of the Advisory Editorial Board from the time of its organization and during the earlier years in particular proved a good friend by his advice and counsel. Dr. Hirst occupied a unique position in the profession, he combined with his extensive knowledge of the science of medicine, a cultural and personal quality which is essential and most desirable in the equipment of a physician. He was a physician in whom the human side was of equal rank with scientific attainment. We pay honor to his memory.

George W. Kosmak.

Hugo Ehrenfest.

## Original Communications

---

### EXPERIENCE WITH MULTIPLE DOSE ROENTGEN THERAPY IN MALIGNANT DISEASES OF THE UTERUS AND OVARIES\*

WILLIAM P. HEALY, M.D., New York, N. Y.

IN SEPTEMBER, 1932, at the annual meeting of the American Roentgen Ray Society, I gave as my opinion that any further improvement in statistics dealing with end-results in the treatment of cervical cancer by radiation would depend upon our ability to increase the amount of effective radiation reaching the cancer which already had invaded the parametria and at the same time to avoid doing serious damage to the normal tissues by the rays.

A review of the end-results published at that time by various well-established radiation clinics throughout the world indicated that substantially the same percentage of cures was obtained by all. It seemed evident, therefore, that the probable maximum percentage of cures had been attained by the methods of treatment then in vogue.

Interestingly enough, it did not seem to matter much just which plan of radiation therapy was favored by a clinic, as long as the maximum dosage of radiation, within the limits of normal tissue tolerance for adjoining structures, was given to the primary lesion. In the majority of instances this was accomplished by means of radium applied directly to the latter. In some clinics deep x-ray therapy was used in conjunction with radium, usually following it, although in a few clinics two cycles of x-ray were given, one preceding the radium applications and the other following them.

A study of the amount of effective radiation reaching the cancer located in the parametrial tissues by means of the methods of x-ray therapy in use at that time, readily demonstrated that the total dosage was so small as to be almost of negligible value as regards a destructive effect upon cancer, except in the presence of extremely radiation sensitive cancer growths. Its chief value seemed to be in the response obtained from the ulcerated and infected primary lesion which usually cleaned up remarkably under the x-ray so that the subsequent radium applications could be made more effectively and with less risk of local inflammatory reactions, or of causing severe and continuing infection and slough in the necrotic irradiated tissues.

---

\*Presented at the Sixtieth Annual Meeting of the American Gynecological Society, held at Hot Springs, Va., May 27 to 29, 1935.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



Actually, as far as treatment of cancer of the cervix was concerned, the only advantage accruing to clinics with well-organized deep x-ray therapy departments lay in the greater flexibility and range of treatment available for advanced cases and for cases in which one could not expect more than temporary palliation. Such patients stood the x-ray treatments well since it required but a few minutes to give each treatment. In this way the patients in the hopeless cases were probably given a few more weeks or months of useful life than could have been obtained by radium alone.

Accordingly with a view to increasing the amount of radiation reaching the parametrial field, we established a different plan of x-ray therapy in January, 1933, for our cases of cancer of the cervix. Our experience with the first 26 patients treated under this plan was given in a preliminary report read in September, 1933, before the American Congress of Radiology.<sup>2</sup>

. We stated that "Our usual plan of external irradiation with x-rays was changed in order to increase the amount of effective radiation given to the pelvic field adjoining the cervix, with the thought of controlling the disease in advanced cases for a longer period of time, and possibly thereby to lead to an increase in the percentage of permanent cures in such cases."

The method followed in the 26 cases reported consisted in lengthening the target skin distance from 50 cm. to 70 cm. and in giving only 200 r. at one time to a skin field instead of 700 r. Lengthening the target skin distance increased the depth dose, and reducing the number of roentgens for each treatment diminished the skin reaction, thus permitting more treatments to be given to each field, thereby increasing the total number of roentgens given to each skin area. Daily treatments of 200 r. were given to each of two opposite fields until a total of 2,000 r. or in some cases 2,400 r. had been given to each of the four fields.

The x-ray dosage factors in this series were as follows: 200 kv. peak voltage, 30 ma. current, 70 cm. target skin distance, 0.5 mm. cu. + 2.0 mm. al. filtration, two anterior and two posterior fields, 10 × 15 cm. each, 200 r. per treatment.

A total of 400 r. were thus given daily to alternate halves of the pelvis including the corresponding half of the cervix. It required three to four weeks to give this series of treatments and when they were finished it was estimated that from three to five threshold erythema doses of roentgen radiation had been given to the cervix and parametria for a distance of 10 to 11 cm. lateral to the cervical canal. This was considerably more than had been obtained by our previous single cycle plan of 700 r. to each field at one exposure. The latter plan gave 1 to 2 threshold erythema doses throughout the parametria.

This first or experimental series was interesting and instructive to us in that the patients on the whole stood the treatments well. The skin

was not badly damaged, in fact only in 10 per cent was there a marked reaction with blistering and peeling. Bladder irritability except for temporary increased frequency was unusual. Intestinal disturbance was more constant. As a rule it was shown by diarrhea and cramps for a week or ten days but in a few instances these symptoms persisted longer and were more severe and caused in such cases considerable prostration and weight loss, nevertheless by hospitalizing such patients they were able to continue treatment.

We were favorably impressed by our experience with this series of cases and by the fact that in 20 of the 26 cases primary healing of the ulcerated, diseased cervix was observed under x-ray alone before radium was applied.

As our experience grew in the use of this so-called multiple divided dose plan of x-ray therapy, we found it desirable to vary the plan according to various controlling factors.

It was our impression that patients in poor or only fair physical condition did better under the single pelvic cycle rather than the multiple dose prolonged treatment plan.

Patients with very advanced disease in which treatment can be regarded only as palliative we believe should not be subjected to this intensive form of radiation therapy. A number of such patients were treated and gave a rather satisfactory and encouraging response for a few months, there was complete local healing with cessation of bleeding and discharge and a distinct gain in weight. After several months however local ulceration occurred again, the patients lost weight very rapidly and suffered intense pain from renewed cancer activity in the fibrosed parametrial tissue resulting from the roentgen radiation.

It is questionable in our minds whether one is justified in subjecting these patients, hopelessly ill with advanced cancer, to the mental and physical strain as well as the financial expense of prolonged radiation therapy when the probable prolongation of life will be so short and the ultimate pain and distress so great. As a result of our experience with such cases during the past two and a half years I have decided not to advise intensive roentgen radiation for them.

As a general proposition because of limited bed capacity in our hospital we prefer to carry on the x-ray treatments with the patients ambulatory and residing outside the hospital. If a patient's residence is more than forty-five to sixty minutes' journey from the hospital, we find it best to give only the single instead of the multiple dose cycle. Patients living near the hospital and in good physical condition may take a prolonged series of treatments. Those in poor condition or living at a distance must have a short series.

Patients with heavy pendulous abdomen or quite generally obese are not good subjects for roentgen radiation. Much skin and subcutaneous fat damage is apt to result, leading to localized areas of brawny indura-

tion with overlying telangiectases. Such areas are easily injured and this may result in chronic ulceration extremely difficult to heal. For these reasons roentgen radiation usually is omitted in obese patients. In re-

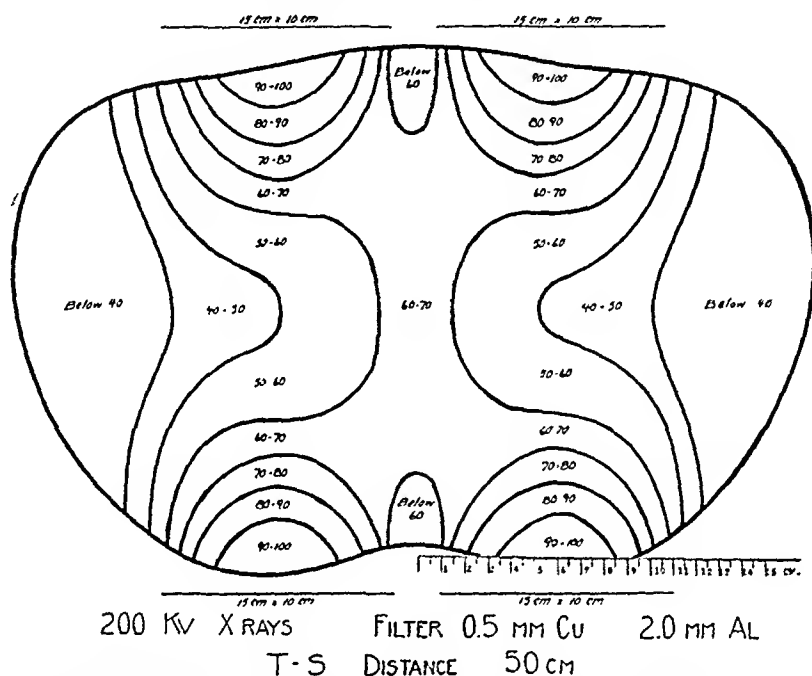


Fig. 1.—The distribution of roentgen radiation obtained within the average female pelvis from four fields of the size and location shown. Target skin distance 50 cm.

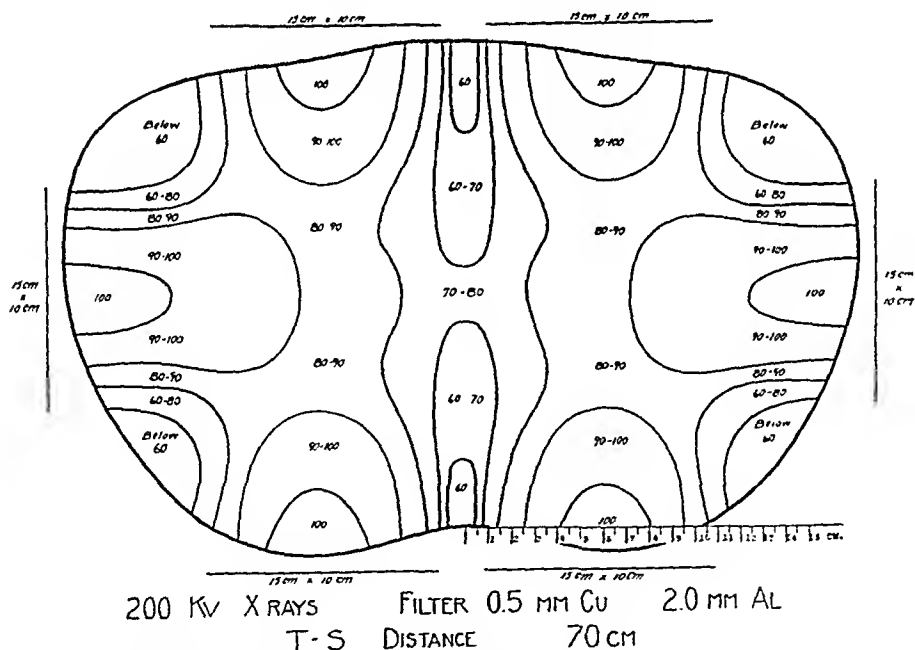


Fig. 2.—The distribution of roentgen radiation obtained within the average female pelvis from six fields of the size and location shown. Target skin distance 70 cm.

viewing our records for the past two and a half years, it is evident at once that these and other factors have guided or influenced us in our choice of the method of roentgen ray therapy for each case. Early in 1934 at the suggestion of Dr. A. Norman Arneson we added a right and a left lateral

pelvic field to the two anterior and two posterior fields previously used. This change was made in order to widen the field of parametrial radiation and to increase the percentage depth dose reaching the tissues in the outer portion of the pelvis.

With the previous set-up of four fields and 50 cm. target skin distance one obtained in the parametrial fields located from 6 cm. to 10 cm. lateral to the cervical canal about 50 to 40 per cent of the skin dosage. Under the new set-up of six fields and treatments given at 70 cm. from 85 to 95 per cent of the total skin dosage is obtained in these areas 6 to 10 cm. lateral to the center of the cervix. This is approximately an increase of 100 per cent in the amount of effective irradiation delivered to the outlying parametria (Figs. 1 and 2).<sup>3</sup>

At the present time, therefore, with few exceptions, all patients receiving roentgen radiation for carcinoma of the cervix are treated through six ports. From Jan. 1, 1933 to May 15, 1935, about 307 patients with carcinoma of the cervix were accepted for treatment. Most of these were primary cases, some were recurrent, a few were so-called prophylactic, following hysterectomy.

Eighty-nine patients received 1 or 2 cycles of 4 fields, 2 anterior and 2 posterior, 200 kv., at 50 cm., 0.5 cu., 2.0 Al., 700 r. each field. As a rule those in which only one cycle was given received it before the radium application and failed to return for the second cycle later on. The parametrial field in such cases therefore received the equivalent of about one threshold erythema dose from the x-ray. In the patients receiving two cycles one was given before and the other about four to six weeks after the radium, the parametrial fields received the equivalent of two threshold erythema doses from roentgen radiation.

Eighty-one patients received two cycles of six fields at 70 cm., 700 r. each, one cycle before and the other following the application of radium. In this group the parametrial tissues also received about two threshold erythema doses but the addition of lateral treatment ports widened out the parametrial fields so that a larger area about 10 by 16 cm. received the equivalent of two threshold erythema doses.

One hundred and seven patients received multiple divided doses of roentgen ray. The dosage factors were 200 kv., 30 ma. current, 70 cm. target skin distance, 0.5 mm. cu., 2.0 mm. Al. filtration, 14 by 10 fields, six fields, 2 anterior, 2 posterior, right and left lateral, 300 r. daily to each of two opposite fields for total of 600 r. daily.

Treatments continued until 1,500 r. to 1,800 r. had been given to each field. This would be equivalent to from  $2\frac{1}{2}$  to  $3\frac{1}{2}$  threshold erythema doses in a parametrial field measuring 10 cm. anteroposteriorly and 16 cm. transversely in an average female pelvis of 23 by 35 cm.

Those patients in whom an effort was made to give a long series of deep x-ray treatments are the ones with which we are chiefly concerned in this study as they are the cases in which the heaviest dosage was given by this method not only to the primary lesion and the parametria but also to the skin, the abdominal walls, the intestines, bladder, blood vessels, nerves, etc.

It should be of interest therefore to note the effect of such treatments on the cancer and on the normal tissues traversed by the rays, also to

determine whether these treatments can be safely given, and to ascertain if the response of the cancer to them is sufficient to justify the increased cost and inconvenience to the patient.

We fully realize it is not an innovation to give multiple divided doses of x-ray for the treatment of cancer. For a long time such treatments have been given by Coutard at the Radium Institute in Paris. While his method is best known because of his work with oral cancer, nevertheless he has also treated many of their cases of cancer of the cervix by means of multiple prolonged exposures to deep roentgen rays and has apparently led to a distinct improvement in the percentage of five-year cures reported by them.

In our work the effort has been made to continue the x-ray treatments in each case up to the limit of tolerance of the normal tissues in the irradiated fields. Since the percentage of radiation reaching the skin is always greater than that received by the underlying tissues we are usually guided in our decision to go on or to stop, by the skin reaction.

With the x-ray dosage factors used in our set-up, the threshold erythema dose is about 500 r. for a single exposure. Since six ports or fields are used and two opposite fields are treated daily, it requires three days to make one complete cycle of the pelvis. Therefore a seventy-two-hour interval elapses before the same skin area is treated again.

Duffy, Arneson, and Voke<sup>4</sup> in their study of human skin recuperation following irradiation concluded that the skin in forty-eight hours recovered 76 per cent of the immediate radiation damage suffered. They estimated that 425 r. would represent the threshold erythema dose for two treatments given at a forty-eight-hour interval. As our patients received only 300 r. every seventy-two hours to the same area with similar x-ray factors to theirs, there was sufficient time for marked skin recuperation between treatments.

With six fields we soon found that skin reactions and intestinal disturbances were more marked and appeared sooner than when only four fields were used. This no doubt is explained by the fact that only twenty-four hours elapse between the anteroposterior and lateral treatments on each side of the pelvis, and this results in cross firing of adjoining fields within twenty-four hours and a piling up of radiation effect in them.

Rarely, however, were the skin reactions alone severe enough during the course of treatment to necessitate postponing or stopping treatments. As it required fifteen to eighteen days to finish the x-ray, the skin changes were usually growing evident toward the end of the series and tended to be much more noticeable in the following two weeks after which time they rapidly subsided.

On the other hand disturbances of the bowel, evidenced by frequent stools and intestinal cramps might occur during the course of x-ray treatments and if not controlled by diet and medication would necessitate omitting the x-ray treatments for several days.

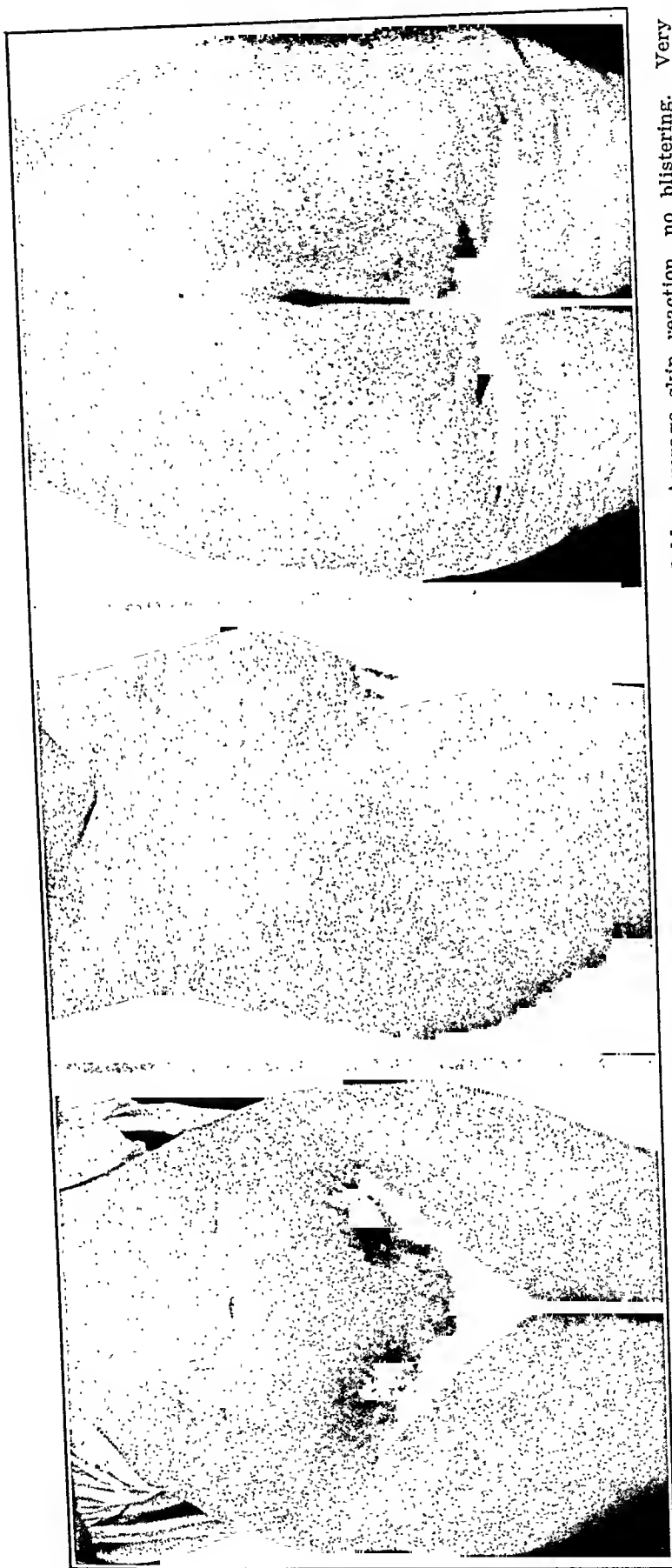


Fig. 3.—A, Anterior fields. Six fields, 70 cm. 300 r.  $\times$  2 fields daily, total 2100 r. each field. Average skin reaction, no blistering. Very advanced cervix case. Complete primary healing with x-ray. Radium tandem 3000 mc. hr. given one month later. Very satisfactory condition, one year later. B, Lateral fields. C, Posterior fields.

However it was more common to have the bowel symptoms make their appearance toward the end of the series, and then they might continue for two to four weeks afterward.

Bladder symptoms, if present at all, were usually mild and rarely required medication. It was not unusual to have a patient suffering from urinary frequency and dysuria caused by the cancer, remark that her bladder symptoms were relieved by the x-ray treatments.

Constitutional symptoms due to anorexia, nausea, vomiting, general prostration, rarely occurred. Strange to say the most severe constitutional, intestinal and skin reactions occurred in the cases in which the radium applications preceded the x-ray. This has been so noticeable in several cases in which x-ray therapy was started two or three days after the radium, because the lesions were not extensive and they were regarded as favorable for immediate application of radium, that I believe the x-ray series should not be started sooner than fourteen days after the termination of radium treatments. This will permit the tissues to recuperate somewhat from the intense reaction caused by radium before they are called on to take care of the x-ray treatments. Heyman<sup>5</sup> who gives a much smaller dosage of x-ray than we do, delays it until three weeks after the radium treatment.

In fact it seems to me quite definite that our advanced cases in which x-ray preceded radium were less disturbed by the combined x-ray and radium applications and went through all of their treatment more readily than the more favorable cases in which the radium treatment preceded the x-ray series.

If this observation is correct, I believe we will be justified in giving the x-ray series first in all cases in which it is to be used. The radium can be applied later.

In their preliminary report, Healy and Arneson<sup>2</sup> drew attention to the opportunity presented for frequent observation and study of the diseased cervix throughout the course of x-ray treatment. This is an advantage which should not be overlooked as it permits one to keep constantly informed as to the progress of the case and its response to radiation.

Dr. Fred Stewart of the Pathological Department who has kindly cooperated in this study by checking the radiation changes in the biopsy specimens, noted in some instances a slowing up in the regression of the cancer cells after a week or ten days of x-ray treatment. Thinking this might indicate greater resistance in the remaining cancer tissues, Dr. Stewart suggested increasing the x-ray dose per treatment in these cases rather than continuing with the same total daily dose throughout the series. In several cases a pyramidal plan of multiple x-ray treatments was followed.

This was a small series of 14 cases. Only 2 anterior and 2 posterior fields were used. The x-ray dosage factors were unchanged. Twelve

patients were given 5 pelvic cycles, 200 r. to each field, 2 opposite fields daily, followed by 5 pelvic cycles, 300 r. each field, 2 opposite fields daily, total r. to each of 4 fields at end of treatments was 2,500. Two patients were given 200 r. for 1 cycle, 300 r. for 4 cycles, and 400 r. for 3 cycles, total dosage to each field 2,600 r.

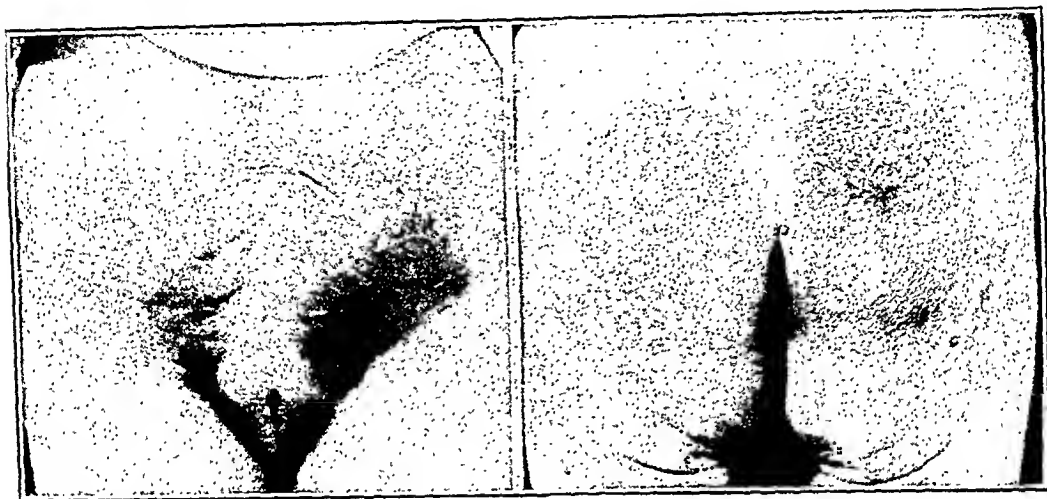


Fig. 4.—A, Anterior fields. Very advanced cervix carcinoma. Four fields at 70 cm., pyramidal method, 200 r.  $\times$  5 = 1000 r., 300 r.  $\times$  5 = 1500 r., 2500 r. to each field. Marked dermatitis. Good primary regression. Photograph taken one week after last x-ray treatment. B, Posterior fields. Photograph taken one week after last x-ray treatment. Marked reaction with mild blistering and peeling.

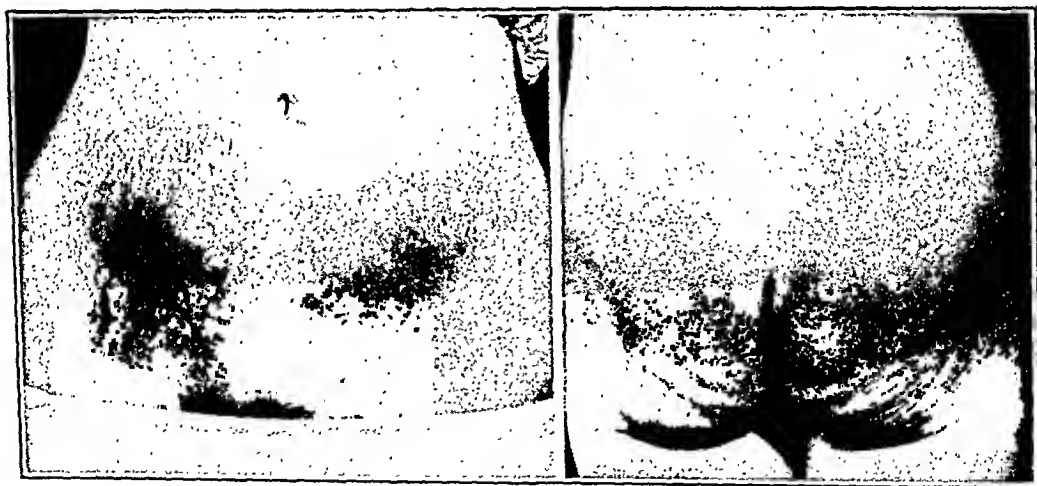


Fig. 5.—A, Anterior fields. Patient V. Q., aged twenty-seven years, had advanced primary cancer of cervix. Six fields 14 by 10, 70 cm., 300 r., two fields daily. Total 1500 r. each field. Photograph taken one week after x-ray. Good skin reaction, no blistering. Complete regression primary lesion in five weeks. B, Posterior and lateral fields. Marked reddening and peeling, no blistering. Photograph one week after x-ray.

One patient in the first series stopped at 1,900 r. because of proctitis and one in the second series at 1,800 r. because of dermatitis. The disease, however, appears to have been controlled in both cases.

All the patients were suffering from advanced cancer of the cervix, 4 of the 14 were classified as very advanced. There were 4 colored patients in the group. With the two exceptions noted above the patients went through with their treatments without undue annoyance. Five of them



are alive and free from evidence of active disease, one has had fair palliation, four are doing badly and four are dead.

No conclusions can be drawn from this group except to say that 12 out of 14 patients or 86 per cent went through with this special form of x-ray dosage without undue difficulty. As to its ultimate value nothing can be said although it seems to offer interesting theoretical possibilities.

In reviewing the entire series of 307 cervix cases from the standpoint of unpleasant or distressing postradiation reactions there are two cases that stand out sharply from the others because of the extreme severity of their symptoms. Each was treated by vaginal and intrauterine application of radium and two days later in one case, three days in the other roentgen ray treatments were begun.

In the first instance a single pelvic application of six fields, 700 r. to each treatment, one treatment daily was given. In the second instance six fields were also treated, 300 r. was given daily to each of two opposite fields. This was continued until 1,500 r. had been given to each of the six fields.

Both patients had sharp skin reactions amounting to peeling and marked pigmentation. The bladder reactions were not severe but nevertheless were annoying. The intestinal disturbances were extremely severe and lasted for several months in each case. As a result the patients were badly prostrated and were bedridden for weeks.

In each instance the primary lesion quickly and completely regressed under treatment.

In both of these patients the radium treatments preceded the roentgen ray and the latter was started after a two-day interval in the first case and a three-day interval in the second case. I believe this is much too soon, especially if one has given a full tissue tolerance dose to the cervix with radium. The reaction to the radium will not have had time to assert itself before the additional effect due to the roentgen ray is added to it. It is probable that in many patients this will be more than the normal tissues in the radium treated field can stand, since they have already been subjected to the maximum dose by radium alone.

I believe we are working in the correct direction when we try to increase the amount of x-ray reaching the parametrial extensions of cervix cancer. The fractionated or multiple dose plan would seem to offer the best method of approach. It is evident that the greatest care has to be exercised in choosing the plan to be followed in each case. The multiple dose plan places much more responsibility upon the physician and the roentgen therapist and requires close supervision of the patient constantly during the treatment.

It is doubtful, however, if we can safely, with our present methods, increase the amount of x-ray reaching the parametria so that it will be effective in destroying metastatic squamous cancer, without at the same

time doing permanent and serious damage to the normal tissues and organs in the irradiated field. It is our impression that the lymph gland metastases of squamous epidermoid cancer are fully as radiation resistant as the primary lesion, if not more so.

At least 6 to 8 threshold erythema doses are required to establish regression of the primary lesion, therefore, it is reasonable to assume that as much will be necessary for control of metastases. Whether or not this amount of radiation could be safely spread over the intestinal field lying in the pelvis is questionable.

There is no doubt that we can improve upon our present technic by increasing still further the target skin distance and the filtration so as to eliminate as far as possible the soft gamma rays. At the same time it may be advantageous to reduce the daily dosage to 100 r. or 150 r. The difficulty with those changes is that they will greatly prolong the time of treatment for each case as well as the cost per patient. It will also reduce the number of patients who can be treated in a busy clinic.

The fractionated dose method we believe offers great opportunities for improving our therapeutic results by prolonging the lives of many patients one to two or more years and by curing a small percentage now lost because the radium and x-ray dosages previously used just failed to be sufficiently adequate to control their disease, especially in the parametrial tissues over an area within 6 cm. of the cervical canal. Even if we cure only three or four more patients in every hundred, it will be an increase of 10 or 15 per cent over our present salvage and the extra effort will be more than worth while. As was intimated above I do not believe we can hope, for the present, to save the lives of many patients in whom there is extensive or palpable disease in the more distant parametrial fields even with prolonged x-ray treatment of the fractionated or multiple dose type.

Our experience in the treatment of metastatic and recurrent ovarian cancer with multiple x-ray treatments has been more satisfactory.

For ovarian cases we use eight treatment fields, 4 anterior and 4 posterior, to cover the abdomen and pelvis, since the secondary tumors may exist any place within the peritoneal cavity.

The usual plan has been to give a treatment of 500 r. to one field daily. The pelvic fields are treated first and the upper abdominal fields next. The treatments are then repeated in the same order until 1,000 r. have been given to each field. This dosage does not seem to be excessive for these patients, although many of them are quite enfeebled by their disease and the presence of abdominal fluid in large amount which may require removal from time to time during the course of x-ray therapy.

The x-ray dosage given in this manner is equivalent to approximately two threshold erythema doses throughout the abdominal and pelvic fields.

Interestingly enough this rather small amount of radiation seems to be adequate to inhibit tumor growth activity in many cases and often

this is followed by complete disappearance of all secondary tumor masses. The primary tumor mass may also be considerably reduced in size but rarely disappears except in the case of anaplastic or embryonal cell tumors.

As soon as the tumor growths begin to regress under radiation, less ascitic fluid is formed, and, therefore, abdominal paracentesis is less frequently necessary. This is one of the first indications that the growths are responding to treatment.

When the patient responds favorably to the first series of x-ray treatments, we do not hesitate to repeat it in three months. At no time in our ovarian tumor cases have we had any unpleasant or serious skin or intestinal complications.

Our experience with deep x-ray therapy in multiple doses in ovarian tumors would indicate that such intraperitoneal metastases or implants are much more radiation sensitive than intraperitoneal metastases from uterine tumors. It is reasonable to assume that this may in part be due to the more delicate structure and high vascularity of the ovarian metastases, as against the more solid, less vascular metastatic squamous carcinoma of the cervix which often is encapsulated within lymph glands.

Some of the most striking cures which we have achieved were obtained by the use of x-ray in multiple divided doses in the treatment of apparently incurable cases of embryonal ovarian tumors in young women.

Our great disappointment has been our failure to control metastatic uterine cancer.

#### CONCLUSIONS

Our experience with multiple dose x-ray therapy for carcinoma of the cervix during the past two and a half years has been encouraging.

A satisfactory technique of x-ray dosage and treatment factors still needs to be developed.

Although we are at the present time giving 300 r. daily to two opposite fields we have not as yet determined that this is the optimum dose. Nor have we determined the optimum rate of administration.

The multiple divided dose method of x-ray therapy cannot be used to advantage for all cervix cases. It is desirable to choose with great care the cases in which it is to be used. By this method of careful selection, I believe, we will cure many patients who now die in the third and fourth years under our present methods of radiation therapy.

There is still much to be learned regarding x-ray therapy, and it offers an interesting and fruitful field for study and experiment.

#### REFERENCES

- (1) *Healy, William P.*: Am. J. Roentgenol. 31: 60, 1934. (2) *Healy, William P., and Arneson, A. N.*: Am. J. Roentgenol. 32: 646, 1934. (3) *Arneson, A. N., and Quimby, E. H.*: Radiology 25: 182, 1935. (4) *Duffy, J. J., Arneson, A. N., and Foke, E. L.*: Radiology 23: 486, 1934. (5) *Heyman, J.*: Acta radiol. 16: 129, 1935.

## PHYSIOLOGIC CHANGES OCCURRING IN THE URINARY TRACT DURING PREGNANCY\*

J. MASON HUNDLEY, JR., M.D., HENRY J. WALTON, M.D.,  
JOHN T. HIBBITTS, M.D., ISADORE A. SIEGEL, M.D., AND  
C. BERNARD BRACK, M.D., BALTIMORE, Md.

(From the Departments of Gynecology, Roentgenology, and Obstetrics of the University of Maryland, and the Department of Gynecology of the Johns Hopkins University)

FOR many years it has been known that dilatation of the kidney pelvis and ureter occurs during pregnancy. This observation, particularly as to its etiology, has been of special interest to obstetricians, urologists, and pathologists. Among the outstanding early investigators in this subject was Pierre Rayer, who, in his *Maladies des Reins* in 1841, called attention to the occurrence of dilatations in the urinary tract during pregnancy and the frequent presence of an associated infection. Another early observer was Cruveilhier, who showed in his *Descriptive Anatomy* 1843, that dilatations of the ureters occurred in all women who died following confinement or during the latter months of pregnancy. Due to the interest aroused by these findings, many men were stimulated to investigate the cause of these changes, and from then on, articles began to appear in the literature. Opitz, in 1905, presented a paper on "Pyelonephritis of Pregnancy and Puerperium" in which he stated that pyelonephritis occurs more frequently in the second half of pregnancy and is probably due to the compression of the ureter by the enlarging uterus at the pelvic brim, with subsequent dilatation of the urinary tract. With congestion thus brought about, infection may be established by organisms ascending from the bladder with the development of pyelitis or pyelonephritis. He was the first to advance the theory that pressure was the causative factor in ureteral dilatation with pregnancy.

In spite of the large amount of work done on the etiology of these dilatation changes, no one has yet, to our knowledge, been able to produce incontrovertible proof as to the cause of this condition.

Our interest was first aroused in this subject by the constant finding of marked dilatation of the pelvis and ureter in all cases of pyelitis of pregnancy. We were then of the opinion that these conditions were caused primarily by an infectious process with a subsequent development of these dilatation phenomena. From the information obtained from this investigation, we now feel that the dilatation and stasis come first and the infection is superimposed upon it.

\*Read, by invitation, at the Sixtieth Annual Meeting of the American Gynecological Society, Hot Springs, Va., May 27 to 29, 1935.

In order to make a thorough study of the problem from every viewpoint, the following program of investigation was undertaken.

1. An intravenous urographic study of the urinary tract changes occurring in normal women during the succeeding months of pregnancy and the puerperium.
2. Obstetric observations of interest.
3. Investigation of urinary tract changes with the use of the indwelling catheter.
4. Urographic study associated with large pelvic tumors; pre- and postoperative manifestations.
5. Histology of the ureter during pregnancy.
6. Observations on the urinary tract of spayed dogs being subjected to prolonged injections of amniotin.

#### 1. INTRAVENOUS UROGRAPHIC STUDY DURING PREGNANCY AND THE PUERPERIUM

Kretschmer and Heaney were the first to report in 1925, their observations on urinary tract changes during pregnancy by the use of retrograde pyelography. These investigators concluded that varying degrees of dilatation occurred in 80 per cent of normal pregnancies.

Three years later, Duncan and Seng contributed an exhaustive study of seventy-eight normal pregnant women who were examined by retrograde pyelography throughout the succeeding months of pregnancy and during the puerperium. The observations during pregnancy began at the sixth week and continued to term; whereas, the postpartum series began on the ninth day and continued to the twenty-fifth day. A summary of their conclusions is as follows: A dilatation of the right ureter was found in every case of pregnancy examined; whereas, the occurrence of right hydronephrosis was only slightly less frequent. The dilatation of the left urinary tract was not of such frequent occurrence. The multiparous woman showed these dilatation changes earlier, more frequently, and to a greater degree than did the primipara.

Every pregnant woman has some degree of obstruction with urinary stasis and resulting dilatation. A high percentage of normal pregnant and puerperal women have pus and "coliform organisms" in the urine.

With the introduction of intravenous urography, an increasing amount of investigative work has been done on the urinary tract during pregnancy. This safe and simple method of urography has been made possible by the pioneer work of Rowntree, Osborne, Sutherland and Scholl, working at the Mayo Clinic during 1923. They were the first to show that the renal pelvis and the bladder could be outlined following the intravenous injection of large doses of sodium iodide. However, it soon became evident that if this diagnostic method was to be universally adopted, a more tolerant substance than sodium iodide would have to be found. Through the efforts of Binz and Raeth of Berlin, a combination of iodine in high concentration with a pyridine ring was elaborated. Swick, in 1929, recognizing the possible value of this substance, known as selektan neutral, in pyelography, became associated with von Lichtenberg, and with the assistance of Binz, a nontoxic substance suitable for intravenous urography was developed. The substance was known as uroselektan.

Among the many investigators working on the urinary tract changes, Duncan and Seng, Lee and Mengert, P. Schumacher, Hofbauer, Dugald Baird, Kretschmer and Heaney may be mentioned.

It will suffice to briefly report the results of two thorough studies whose findings are generally similar to those obtained by other workers in this field.

Kretschmer, Heaney, and Ockuly, wishing to verify their results, reported in 1925, by the use of intravenous urography, studied thirty-one normal women throughout pregnancy and the puerperium, until the urinary tract had returned to normal. They also showed that as a rule the dilatation was progressive and that the presentation and position of the fetus showed no causal relationship to the dilatation or displacement.

Paul Schumacher (*Arch. f. Gynäk.* 143: 28, 1930), reports his observations on the study of one hundred normal pregnant women. He finds that during the first four months of pregnancy, the ureters preserve their normal course. During the fifth and sixth months in 50 per cent of cases, and during the seventh and eighth months in 80 per cent, there is an alteration in the direction of the lower part of the abdominal ureter. This is displaced outwards and backwards and comes to lie on the lateral slope of the psoas muscle and may have a convexity directed outward. The relations of the pelvic ureter show little disturbance by the growing uterus. Of the one hundred cases, there was a dilatation of both ureters in 83 cases, 15 of the right ureter only, and 2 of the left ureter only. The dilatation may reach a radius of 2 to 2.5 cm. and affects both primiparas and multiparas. Ureteral kinks were almost constantly found and were usually located just below the renal pelvis.

In order for us to make a thorough investigation of the dilatation phenomena occurring in pregnancy, it was necessary to study the changes throughout the entire course of gestation as well as in the puerperium. We were particularly interested in studying the causation of the ureteral changes and wished to test out some of the theories advanced, but we also wished to observe how soon deviations from the normal were noted, whether the dilatations were progressive and how soon retrogression took place.

It was decided that the closely related problem of pyelitis of pregnancy would not be taken up in this article but would be considered in a later publication.

For the sake of clarity, and in order to make certain deductions, it was decided to present and classify our findings according to three separate groups, namely: Stage 1: Changes occurring up to the fifteenth week of pregnancy; Stage 2: changes occurring from the fourth month up to delivery; Stage 3: changes during the puerperium.

This study was begun with thirty-five normal pregnant women who had no past history of any urinary infection, and whose urine was microscopically and culturally normal. However, for several reasons, such as development of nephritis early in pregnancy, pyelitis, failure to return, etc., eight patients were discarded, so that twenty-seven remained for a complete study. Of these, twenty were primiparas and seven were multiparas. Their ages ranged from sixteen to thirty-one years.

Through the generosity of the Winthrop Chemical Company, sufficient Neoskiadan, now known as Diodrast, was gratuitously supplied to make this study possible. The following was the method of procedure used. Twenty cubic centimeters of neoskiadan were slowly injected into the median basilic vein. The number of injections given in

all was 172, and at no time was a reaction of any consequence produced. If the solution was injected quite slowly, the only sensation experienced was that of diffuse body warmth; however, if it was given rapidly, the patient complained of nausea and at times vomiting occurred. The reactions were very transitory, lasting less than one minute. In two cases, some of the fluid was known to have escaped into the tissues of the arm during the injection, but no reaction of any kind developed. The first x-ray was taken fifteen minutes following the injection of neoskiadan, and subsequent exposures were made at fifteen-minute intervals. As pregnancy and dilatation changes in the urinary tract progressed, it was found that the excretion time was delayed and frequently a delay of thirty to forty-five minutes was necessary before a satisfactory film could be obtained. It was noted that the more marked the dilatation, the greater the delay in the excretion time; this resulted in the earlier appearance of the dye in the more normal side. Following delivery, it was necessary to take the first film as early as seven minutes after the intravenous injection, for if there was much delay, most of the dye was found in the bladder. This was due to the absence of urinary stasis, atony, and the return of the excretion time to normal. Urographic studies were made at intervals of six to eight weeks up to the time of delivery; they were then continued postpartum, until the urinary tract had returned to normal.

#### ANALYSIS OF RESULTS

*Stage 1.*—This portion of the study comprises examination of early pregnancies up to the fifteenth week. In this group there were thirteen patients examined, ten of whom were normal and only three showed slight changes in the urinary tract prior to the fifteenth week of pregnancy. Of these three, one examined at the ninth week showed dilatation, tortuosity and outward displacement of the right ureter. Another studied at the fourteenth week demonstrated dilatation of the right kidney pelvis as well as dilatation of both ureters. The remaining patient examined at the twelfth week showed the left kidney pelvis dilated.

*Stage 2.*—This period of investigation includes examinations from the fifteenth week of pregnancy to term. In this group there were twenty-seven patients studied and the following facts were brought out:

Dilatation of the pelvis and calyces of right kidney, 24 cases, 88.8 per cent.

Dilatation of right ureter, 25 cases, 92.8 per cent.

Dilatation of pelvis and calyces of left kidney, 6 cases, 22.2 per cent.

Dilatation of left ureter, 17 cases, 63.2 per cent.

Lateral displacement of right lumbar ureter, 7 cases, 25.8 per cent.

Lateral displacement of left lumbar ureter, 18 cases, 66.6 per cent.

*Stage 3.*—This final period of study began the seventh day postpartum and continued until the examinations showed a complete return to normal. All of the patients except one were examined during this period. The tabulated results follow:

On the seventh day postpartum, the urinary tracts of 8 patients had returned to normal.

On the tenth day postpartum, the urinary tracts of 2 patients had returned to normal.

On the fourteenth day postpartum, the urinary tracts of 3 patients had returned to normal.

On the twenty-first day postpartum, the urinary tract of 1 patient had returned to normal.

On the twenty-eighth day postpartum, the urinary tracts of 4 patients had returned to normal.

On the thirty-fifth day postpartum, the urinary tracts of 4 patients had returned to normal.

On the forty-second day postpartum, the urinary tracts of 3 patients had returned to normal.

On the fifty-sixth day postpartum, the urinary tract of 1 patient had returned to normal.

One patient was not examined following delivery.

From this study we find that the most constant change in the urinary system was a dilatation of the pelvis and calyces of one or both kidneys; a dilatation and tortuosity and kinking of one or both ureters, and a lateral displacement of these structures. Every case showed some deviation from the normal, ranging from a slight dilatation to a marked degree of hydronephrosis and hydroureter. The right kidney and ureter were affected more often than the left, but the left ureter was displaced laterally more frequently than the right. One of the most striking findings was that the portion of the ureter which runs over the pelvic wall was not visualized; whereas, the pelvic ureter was often well outlined. In not one of the cases was there found a definite and significant dilatation of the pelvic portion of the ureter. In Stage 1, examinations from the ninth to fifteenth week, there were thirteen patients studied and the pelvic ureter was visualized in all but one. Eleven of these showed some lateral displacement, while in two, slight tortuosity of the left ureter was noted. Only three showed slight dilatation of this pelvic portion of the ureter, two being on the right and one on the left. This latter finding is of special interest when considered in relation to Hofbauer's theory in regard to the etiology of ureteral dilatation.

With the advance of pregnancy, the dilatation of the ureter and pelvis gradually increased. We were unable to observe that the dilatation reached its maximum degree some weeks antepartum and then remained stationary until delivery. We feel that it is a gradually progressive dilatation.

Following delivery there is a return of the urinary system to normal. According to our findings and those of Duncan and Seng, the regressive changes do not seem to be so rapid as some authors state. We found that in twenty-six patients examined after delivery, eighteen of these showed a return to normal in twenty-eight days. However, one case required fifty-six days. These findings are somewhat similar to those of Duncan and Seng, who, in their postpartum study of thirty-six patients, found that from the ninth to the twenty-fifth day, a minority of the cases had returned to normal; whereas, a good majority still showed dilatation phenomena.

It is a well-known fact that the presence of frank infection greatly retards and delays the normal involution processes. However, these cases studied were normal and showed no signs of an inflammatory process.



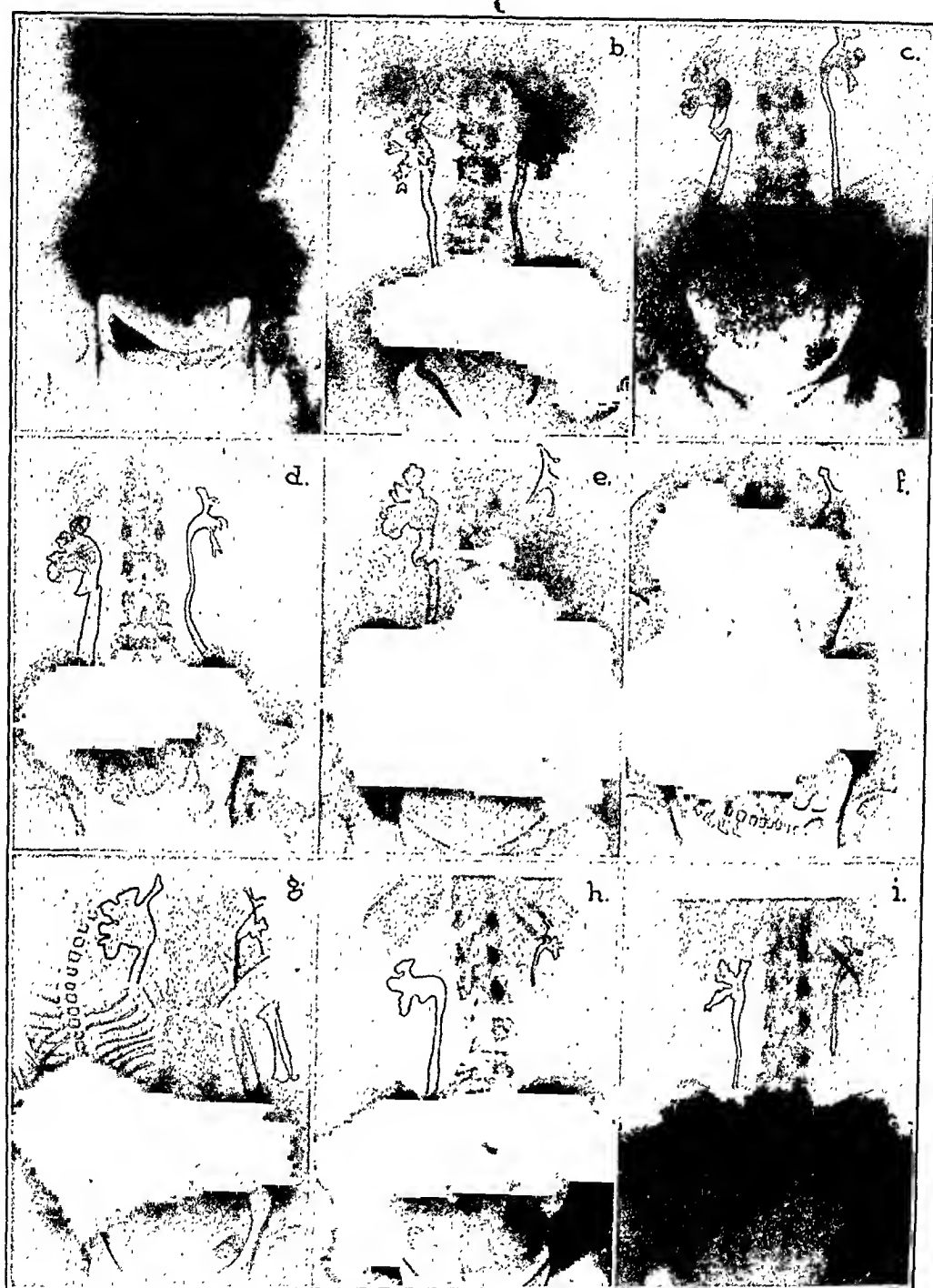


Fig. 1.—*a*, E. C. May 5, 1933. Normal pregnancy illustrating the distance between the head and the superior surface of the bladder. This has been a frequent finding and is not diagnostic of placenta previa.

*b*, A. P. Case 1. Fifteen weeks. Moderate dilatation of both pelvis and lumbar ureters. Also slight dilatation of the right pelvic ureter. Fetus visualized in the pelvis.

*c*, M. L. Case 16. Eighteen weeks. Dilated pelvis and calyces of right kidney. Dilated and tortuous right ureter. Dilatation beginning at brim of pelvis. Slight dilatation of left lumbar ureter. Saucer-shaped depression of bladder. Fetus visualized in pelvis.

*d*, M. L. Case 16. Twenty-two weeks. Increasing dilatation of right pelvis, calyces, and lumbar ureter. Slight dilatation of left lumbar ureter with beginning outward displacement. Fetus well visualized in pelvis.

*e*, M. L. Case 16. Twenty-six weeks. No increase of dilatation of right pelvis, calyces, and ureter since last examination. Fetus visualized, breech presentation, spine to the left.

(Continued on opposite page.)

## 2. OBSTETRIC OBSERVATIONS

It was observed that the dilatation of the urinary tract occurred earlier in the multiparas than in the primiparas. All of the patients studied delivered normally, and there was no case of placenta previa found.

Early visualization of the fetus, during the routine study, was possible in most cases. In thirteen patients, the fetal skeleton could be demonstrated before the fifteenth week, three of these being seen by the tenth week. The position of the fetus changed very frequently, even during the later weeks of pregnancy. In only four cases was the fetus in the same position in the uterus in all examinations. At one x-ray examination, the fetus changed from a vertex to a breech presentation during the fifteen-minute interval between exposures. Owing to this frequent change of presentation, we do not believe that the fetal position has any bearing upon the dilatation changes observed in the urinary tract.

The presence of the placenta previa at times is extremely difficult to determine, and any safe procedure that would aid in the diagnosis of this anomaly would be greatly welcomed.

Menees, Miller, and Holly in 1930, introduced what they termed amniography, a method comprising the injection of strontium iodide solution, as a contrast medium, into the amniotic sac, through the abdominal wall and uterine wall, in order to show by x-ray the position of the placenta. They carried out their observations on twenty-one patients with no injurious or toxic effects to the mother or fetus in normal pregnancies. In one case of placenta previa, at the sixth month, the fetus was expelled about thirty hours after the injection.

Kerr and Mackay in 1932 carried out the same work using uroselectan B in place of strontium iodide, with no harmful effects on mother or fetus. They concluded that the position of the placenta could be determined by this method, but only patients in the latter weeks of pregnancy should be so investigated, as the injection predisposes to the induction of labor.

Recently, Ude, Weum, and Urner have described a roentgen finding which they think is diagnostic of placenta previa. They call attention to the following observation. With the advancement of pregnancy, the enlarging uterus presses down against the bladder, with a resulting concave, saddle depression of its superior surface. They have found that the instillation of a small quantity of sodium iodide into the bladder is helpful in its visualization. The diagnosis is dependent on the anatomical relationship between the fetal head lying in the lower uterine segment and the upper surface of the bladder. They state that the bony outline of the fetal head should be separated from the outline of the bladder only by the thickness of the uterine and bladder walls and the fetal scalp. In the case presented, they found the distance from the bony outline of the fetal head to the crescentic shadow of the bladder to

---

*f*, M. L. Case 16. Thirty-four weeks. Increasing dilatation of the right pelvis, calyces, and ureter. Left kidney and ureter appear normal. Fetus is visualized, breech presentation, spine to the right.

*g*, M. L. Case 16. Thirty-nine weeks. No increase of dilatation of the right pelvis, calyces, and ureter since last examination. Left kidney and ureter appear normal. Position of fetus: vertex presentation, spine to right.

*h*, M. L. Case 16. One week after delivery. The pelvis and calyces of the right kidney have returned to normal but there is still a moderate dilatation of the right ureter.

*i*, M. L. Case 16. Six weeks after delivery. The right pelvis, calyces and ureter are now normal.

NOTE: Urograms outlined for better reproduction.

be approximately 1 cm. This space was thought to be occupied by the placenta and a diagnosis of placenta previa was made and corroborated by cesarean section.

Our findings are not in accord with the above report. In ten of the twenty-seven patients studied, there was found a space between the shadow of the fetal head and the outline of the bladder which varied from 1 to 2.5 cm. in diameter. In none of the patients was placenta previa found, all having normal deliveries. Therefore, we do not feel that this finding is diagnostic of placenta previa (see Fig. 1, *a*, showing distance between fetal head and upper border of the bladder).

We now wish to present a series of illustrations depicting the varying changes in the urinary tract during pregnancy. Fig. 1, *b* shows beginning dilatation of the ureters and pelvis of both kidneys at the fifteenth week of pregnancy. The following seven illustrations are succeeding examinations of the same patient, beginning at the eighteenth week of pregnancy and continuing until the sixth week postpartum (see Fig. 1, *c*, *d*, *e*, *f*, *g*, *h*, *i*).

### 3. INVESTIGATION OF URINARY TRACT CHANGES WITH THE USE OF THE INDWELLING CATHETER

Lee and Mengert in 1934 published an excellent article concerning the effect of pregnancy on the urinary tract. They investigated the debated question of pressure as the etiologic factor in the production of dilatation changes. They logically deduced that if these dilatations were produced by pressure, the relief of this pressure should allow the urinary tract to return to normal.

Their investigations were carried out on fifteen normal women in the last months of pregnancy. A retrograde pyelogram was done and the catheter allowed to remain in the ureter for a period of twenty-four hours, so that there could be continuous urinary drainage. In this way, the effects of stasis and back pressure from compression, if it existed, would be entirely relieved and the dilated tract would show definite evidence of returning to normal. However, none of their cases showed any decrease in dilatation by this continuous drainage for twenty-four hours. A number of intravenous urograms were then made on nonpregnant women who presented various types of pelvic pathology, including ovarian cysts, pelvic inflammatory disease, carcinoma of the ovary, and uterine fibroma. From their observations, they are "skeptical that ureteral obstruction, from any cause whatever, is the reason for dilatation of the upper urinary tract in pregnancy."

Being highly interested in the etiology of the dilatations occurring in pregnancy, we decided to repeat this work with the indwelling catheter and see if the results coincided. Our method of procedure was as follows:

Ten normal pregnant women during the last month of their gestation were selected for this study. An intravenous urogram was first done in order to determine which side showed the greatest degree of dilatation. This being decided, the patient was cystoscoped and a No. 9 x-ray catheter was introduced into that ureter which was the most dilated, the catheter passing as far up the ureter as possible. Specimens

and cultures were obtained and the pelvic capacity measured. Sodium iodide, 15 per cent, was then allowed to run in by gravity. On each examination, the top of the column of sodium iodide in the buret was kept at the same height above the level of the patient, so that conditions were similar in all cases. The catheter was then strapped securely to the abdomen. Liquids were forced and once every twelve hours 5 c.c. of silver nitrate solution (1-1,000) were injected into the catheter, as a prophylactic measure. During the examinations of our first cases, the second pyeloureterogram was made twenty-four hours after the first, but we soon found that sufficient time had not elapsed to show regressive changes in the urinary tract. We discontinued the second x-ray at the twenty-four-hour interval and extended the time for the second pyelogram so that it was done forty-eight hours after the first. We now noticed that a definite diminution in the degree of dilatation of the pelvis and ureter had taken place. In several patients in whom the decrease of dilatation at the forty-eight-hour period was not absolutely definite, the catheter was left in situ for another twenty-four hours. With this additional period of drainage, the diminution in capacity became more marked. The rapidity with which the dilatation decreased varied in different cases, which observation coincided with the usual course of events following delivery.

#### ANALYSIS OF RESULTS

With continuous urinary drainage through the indwelling catheter for a period of forty-eight to seventy-two hours, a definite diminution in the size of the upper urinary tract occurred. It was found that drainage for a period of twenty-four hours was not sufficient to produce these regressive changes.

We were able to show a definite diminution in size of the dilated urinary tract in seven patients. In the remaining three, the following observations were made: In one, who delivered seven hours following cystoscopy, it was found impossible to introduce a catheter up the right ureter due to the pressure of the descending fetal head. One patient delivered thirty-six hours following the introduction of the catheter into the right ureter. The second urogram made at the first twenty-four-hour interval showed no signs of involution. However, the next retrograde pyelogram made twelve hours following delivery, the catheter having been reinserted, showed definite but early signs of a diminution of dilatation (see Fig. 2, *a* and *b*). The remaining patient delivered thirteen and one-half hours after the catheter was inserted. Through error, the indwelling catheter was left in situ during labor. On the following day, cystoscopy showed a line of hyperemic mucosa over the intramural portion of the ureter in which the catheter lay. This graphically illustrated the force exerted against the bladder by the descending head.

We will now show several urograms depicting the changes occurring in the urinary tract with prolonged urinary drainage.

R. G. (Fig. 2, *c*.) Base of pelvis measures 45 mm. Diameter of upper third of ureter is 11 mm. Diameter of middle third of ureter is 15 mm.

R. G. (Fig. 2, *d*.) Forty-eight hours later. Base of pelvis measures 35 mm. Diameter of upper third of ureter is 5 mm. Diameter of middle third of ureter is 11 mm.

H. R. (Fig. 2, *e*.) Base of pelvis measures 21 mm. Diameter of upper third of ureter is 14 mm.

H. R. (Fig. 2, *f*.) Forty-eight hours later. Base of pelvis measures 17 mm. Diameter of upper third of ureter is 9 mm. Diameter of middle third of ureter is 16 mm.

H. R. (Fig. 2, *g*.) Twenty-four hours later. Base of pelvis measures 16 mm. Diameter of middle third of ureter is 7 mm.

E. D. (Fig. 3, *a*.) Base of pelvis measures 5.2 cm. Diameter of upper third of ureter is 1.9 cm. Capacity is 46 c.c.

E. D. (Fig. 3, *b*.) Forty-eight hours later. Base of pelvis measures 4.5 cm. Diameter of upper third of ureter is 1.5 cm. Capacity is 40 c.c.

E. D. (Fig. 3, *c*.) Twenty-four hours later. Base of pelvis measures 4 cm. Diameter of upper third of ureter is 9 cm. Capacity is 21 c.c.

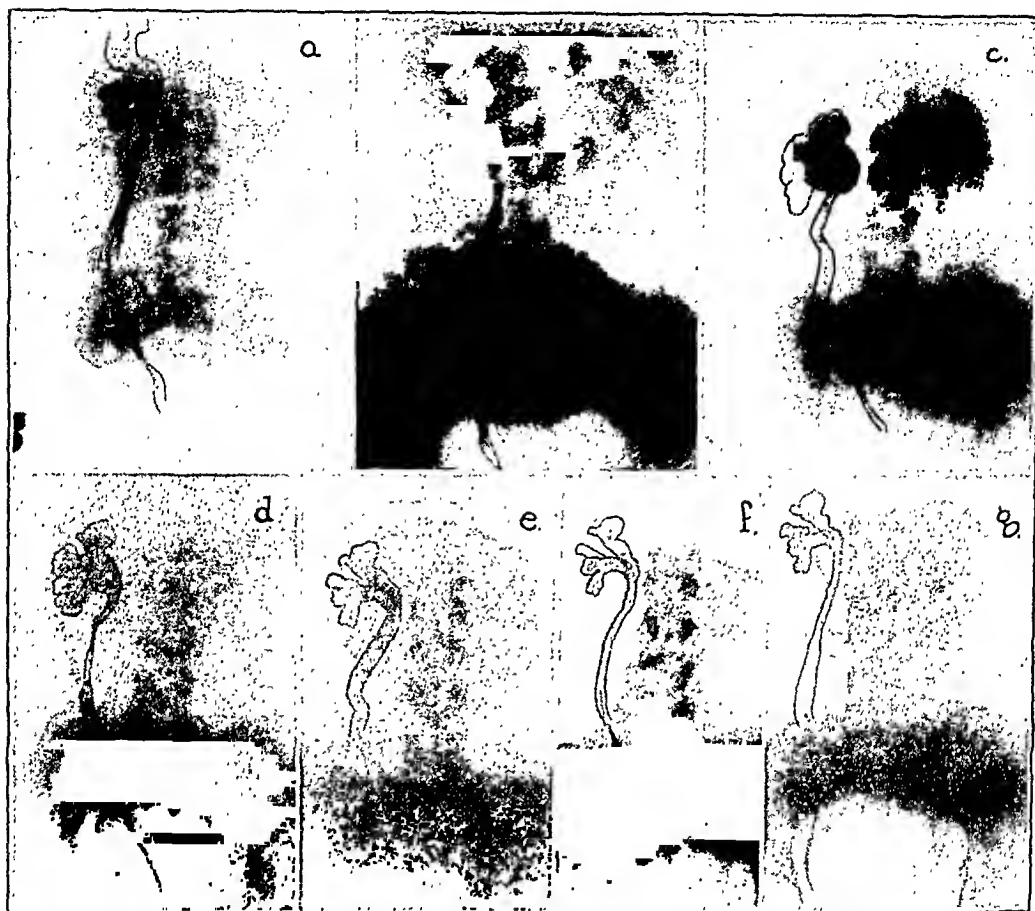


Fig. 2.—*a*, L. A. Jan. 19, 1934. Right kidney shows a marked hydronephrosis. Before delivery, the right ureter is dilated, nodular, and displaced laterally.

*b*, L. A. Jan. 23, 1934. Illustration twelve hours postpartum showing regression in the size of the pelvis, calyces, and ureter. No lateral displacement.

*c*, R. G. Indwelling catheter. April 4, 1934. Right kidney shows marked hydronephrosis and hydroureter. Indwelling catheter extending nearly to renal pelvis.

*d*, R. G. Indwelling catheter. April 6, 1934. In forty-eight hours, there is noted a definite regression in the size of the pelvis, calyces, and ureter.

*e*, H. R. Indwelling catheter. Dec. 17, 1934. The right kidney shows a moderate hydronephrosis. The right ureter is markedly dilated, tortuous, and laterally displaced. Indwelling catheter seen in upper end of ureter.

*f*, H. R. Indwelling catheter. Dec. 19, 1934. In forty-eight hours there is noted a diminution in size of the pelvis, calyces, and ureter.

*g*, H. R. Indwelling catheter. Dec. 20, 1934. Twenty-four hours later there is seen a still greater diminution in size of the pelvis and calyces.

#### 4. UROGRAPHIC STUDY ASSOCIATED WITH LARGE PELVIC TUMORS, PRE- AND POSTOPERATIVE CHANGES

Having shown the changes that take place in the urinary system associated with pregnancy, we felt that it would be of interest as well as instructive to observe what effect, if any, occurred in the presence of pelvic tumors.

Recently, Baker and Lewis have reported their findings based on a comparative study of the urinary tract with pregnancy and also with pelvic tumors. They found

dilatation effects in all sixteen cases with large pelvic tumors, eight of which were ovarian cysts. They were of the opinion that mechanical pressure was the etiologic factor in the production of dilatation phenomena.

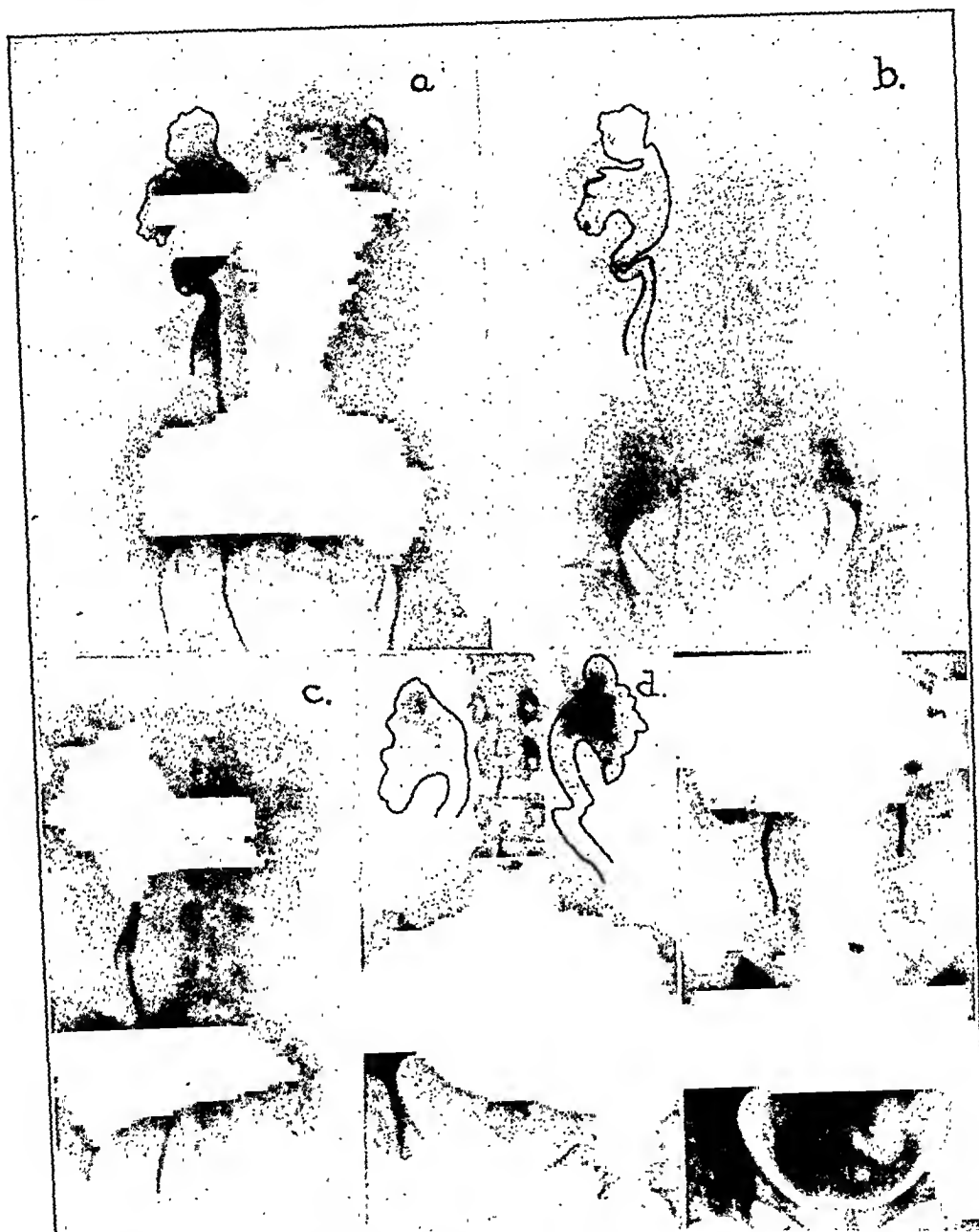


Fig. 3.—a, E. D. Indwelling catheter. Feb. 28, 1934. Right kidney shows a marked hydronephrosis and hydroureter, indwelling catheter tip being in upper end of ureter.  
b, E. D. Indwelling catheter. March 2, 1934. In forty-eight hours, there is noted a moderate dilatation of pelvis, calyces, and ureter.  
c, E. D. Indwelling catheter. March 3, 1934. Twenty-four hours later there is noted an marked dilatation of pelvis, calyces, and ureter.  
d, B. S. Feb. 11, 1935. Fibroid tumor filling pelvis, before operation. Marked dilatation of the pelvis and calyces of both kidneys and both ureters.  
e, B. S. March 21, 1935. (Thirty-eight days later) after operation. Pelvis and calyces of both kidneys and ureters have returned to normal.

Our observations were carried out on a small series of large pelvic tumors, but sufficient in number to well illustrate what associated changes occurred in the urinary tract. Of the eight cases studied, six were large

fibroid tumors of the uterus, one an extremely large fibroma of the left ovary and the remaining patient had a fixed tumor which nearly filled the pelvis; on operation this proved to be a papillary carcinoma of the ovary. Every patient studied; with the exception of the one with the carcinoma of the ovary, showed dilatation effects in the urinary tract which were somewhat similar to those occurring during pregnancy. The main points of similarity were dilatation of the upper tract and delayed excretion time which returned to normal when the obstruction was removed. Intravenous urograms were made before and after operation. With the relief of pressure and the absence of urinary stasis due to removal of the tumor, it was remarkable to observe the resiliency and recuperative powers of the urinary tract. Figs. 3, *d* and *e* strikingly demonstrate how the urinary tract returns to normal. The patient of whom these films were shown stated that the pelvic mass had been present, to her knowledge, for at least three years. At operation, the spherical, fixed, uterine fibroma snugly filled the pelvic bowl and extended up to the umbilicus. It seems evident that pressure must be the cause of these dilatation changes, for here we have a dense pelvic tumor increasing in size and confined in an inelastic pelvis. And then witness the prompt regression of the tract after this obstruction has been removed. Of course, these tumors must be similar in size and contour to the pregnant uterus if they are to produce these dilatation effects.

##### 5. HISTOLOGY OF THE URETER DURING PREGNANCY

During the past year, we have studied histologically the urinary tracts in thirteen women, all of whom excepting two died at term. One of these succumbed following an operation for ectopic pregnancy of six to seven weeks' duration. The other died at six months, of lobar pneumonia. This patient alone showed an infectious process in the urinary tract, multiple punctate abscesses being found in the cortex of the kidney. However, the bladder and ureters showed no evidence of inflammation.

In every case but one, some dilatation of the ureter was found, the right side being constantly more dilated than the left. It is frequently stated that the dilated, tortuous and kinked ureters occurring with pregnancy are longer than those not so associated. However, this has not been our observation. The longest ureter was found to measure 30 cm., and the shortest measured 17 cm. The average length was from 24 cm. to 28 cm. The sacculated dilatations of the upper ureter give one the impression that there is elongation of the tract, which is not borne out by actual measurement.

The gross appearance of the ureters associated with pregnancy had many points in common. As mentioned above, they all showed some degree of dilatation, usually on the right side, which always began above the brim of the pelvis. The lower end of the pelvic ureter was quite firm and rigid; whereas, the abdominal spindle was always flaccid and

ribbon-like, with definite loss of tone. In the upper part of this abdominal portion, one to three sacculations were observed which often were connected by delicate adhesions. There was no evidence of stricture formation made out either grossly or microscopically. The ureters were measured and sectioned at the following levels: Intramural portion, juxtavesical, midpelvic, brim of the pelvis, midabdominal spindle and the ureteropelvic junction.

In order to contrast the changes occurring during pregnancy with the normal, we studied as controls the urinary tracts of five women dying from other than urinary conditions. We also examined normal male ureters which differed in no way from the female ones.

In Bardeleben's *Handbuch der Anatomie des Menschen*, 1902, Disse has given an excellent anatomical description of the normal ureter and the following account is based primarily on his work. The lumen of this muscular tube is lined with stratified epithelium and when the organ is not dilated, folds of mucosa project into the lumen, giving a stellate appearance; these are absent when the ureter is distended with fluid or is dilated. The musculature of the ureter is composed of three layers comprising an inner and outer longitudinal and a middle circular. The muscle bundles are separated by interspaces which contain connective tissue fibers. The volume of the connective tissue is about equal to that of the muscle bundles. Throughout the abdominal portion of the ureter, the circular layer is well developed; whereas, the inner and outer longitudinal layers, especially the latter, are poorly defined.

The pelvic ureter is of somewhat different appearance. The muscular wall is more compact and with the increasing intermingling of the muscle fibers, it is difficult to distinguish separate layers. Here it is also noted that the muscle fibers lie next to the epithelium of the mucosa, for in this region, the tunica propria is absent. The longitudinal mucosal folds are not seen and the lumen often assumes the appearance of a "Y" formed slit. Just above the bladder in the adventitia, thick longitudinal muscle bundles, which apparently arise from the bladder, are seen. These bundles of muscle are surrounded by connective tissue and nearly encircle the ureter. It has been definitely shown that this structure, known as the ureteral sheath of Waldeyer, does not arise from the bladder but is a development of the outer longitudinal layer of the ureteral musculature. Multiple sections taken from different levels in the lower pelvic ureter show that these longitudinal muscle bundles extend up the ureter only for a distance of 3 to 4 cm. The adventitia about the lower end of the ureter is well developed, which gives added density and rigidity to this portion of the organ and is of great importance in binding the structures together.

In presenting our findings on the histologic changes occurring in the urinary tract during pregnancy, we are impressed with several observations which are constantly present, namely, hypertrophy of the musculature, edema and increased vascularity. These changes are noted in the urethra, trigone, bladder, ureter and kidney pelvis, and evidently go hand in hand with similar physiologic changes occurring in the generative tract during pregnancy. The most striking change seen in the urinary system is the marked hypertrophy of the ureteral sheath of Waldeyer. The degree of hypertrophy naturally varies but it is always present and is equally developed in each ureter. Hofbauer is of the



opinion that hypertrophic alterations in the musculature with hyperplastic changes in the connective tissue, plus the constricting tendency of the hypertrophic ureteral sheath, are essential factors in producing urinary obstruction with subsequent dilatation changes. This theory in relation to our findings will be discussed later.

Fig. 4, *a* shows marked hypertrophy of the ureteral sheath which nearly surrounds the lower end of the left ureter. The longitudinal muscle bundles are seen in the adventitia and are separated from the main muscular wall by a band of connective tissue. There is definite hypertrophy of the muscle fibers seen. However, at no time, in the many sections studied, were we able to demonstrate any new growth of tissue, either connective tissue fibers or nonstriated muscle fibers. Increased vascularity and edema were noted, with resulting loosening of the connective tissue meshes and separation of the muscle bundles.

A section taken from the juxtavesical portion of the right ureter of the same patient, Fig. 4, *b*, is quite similar to that just described. It is interesting to observe that in this patient, with equal development of the ureteral sheath in the lower ends of each ureter, there occurred a marked dilatation of the right ureter from the pelvic brim upward; whereas, there was no dilatation of the left ureter found. If the hypertrophy of the ureteral sheath were the etiologic factor, would there not be an equal dilatation of both ureters with the change occurring at the juxtavesical portion and not at the pelvic brim?

The following photomicrograph, Fig. 4, *c*, demonstrates an extreme degree of hypertrophy of the ureteral sheath.

In Fig. 4, *d*, the absence of hypertrophic changes in the ureteral sheath of a non-pregnant woman is noted. The longitudinal fibers making up the sheath are seen but are quite underdeveloped. The muscular wall is compact, no edema or increased vascularity is noted.

Fig. 4, *e*: Section shows another type of nonpregnant ureter at the bladder. In order to determine the origin of the longitudinal muscle bundles seen in the ureteral sheath, several blocks were taken from the intramural portion of the ureter and multiple sections from these studied.

Fig. 4, *f* very definitely shows that these fibers do not spring from the bladder but consist of the well-developed outer longitudinal muscular layer of the ureter. The ureteral wall is separated from the surrounding bladder musculature by an indefinite layer of connective tissue, making it difficult at times to determine the outer limits of the ureter. The mucosa is seen to be normal, there being no infolding of it in this region. The muscle fibers show the usual hypertrophy accompanying pregnancy and are seen directly adjacent to the epithelium of the mucosa due to the normal absence of the tunica propria in this location.

The next illustration, Fig. 4, *g*, shows the juxtavesical portion of the right ureter, the patient succumbing after an operation for an ectopic pregnancy of seven weeks' duration. There is a definite hypertrophy of the ureteral sheath seen, which demonstrates that as early as the seventh week of gestation, sufficient hormone is elaborated to produce this growth change.

We will now consider the abdominal ureter which, as already stated, differs somewhat from the pelvic portion. As we have shown, the abdominal spindle undergoes constant dilatation changes during the latter months of pregnancy, and reference to Fig. 4, *h* illustrates the findings in the ureter, diameter of which, taken at 14 cm. above the

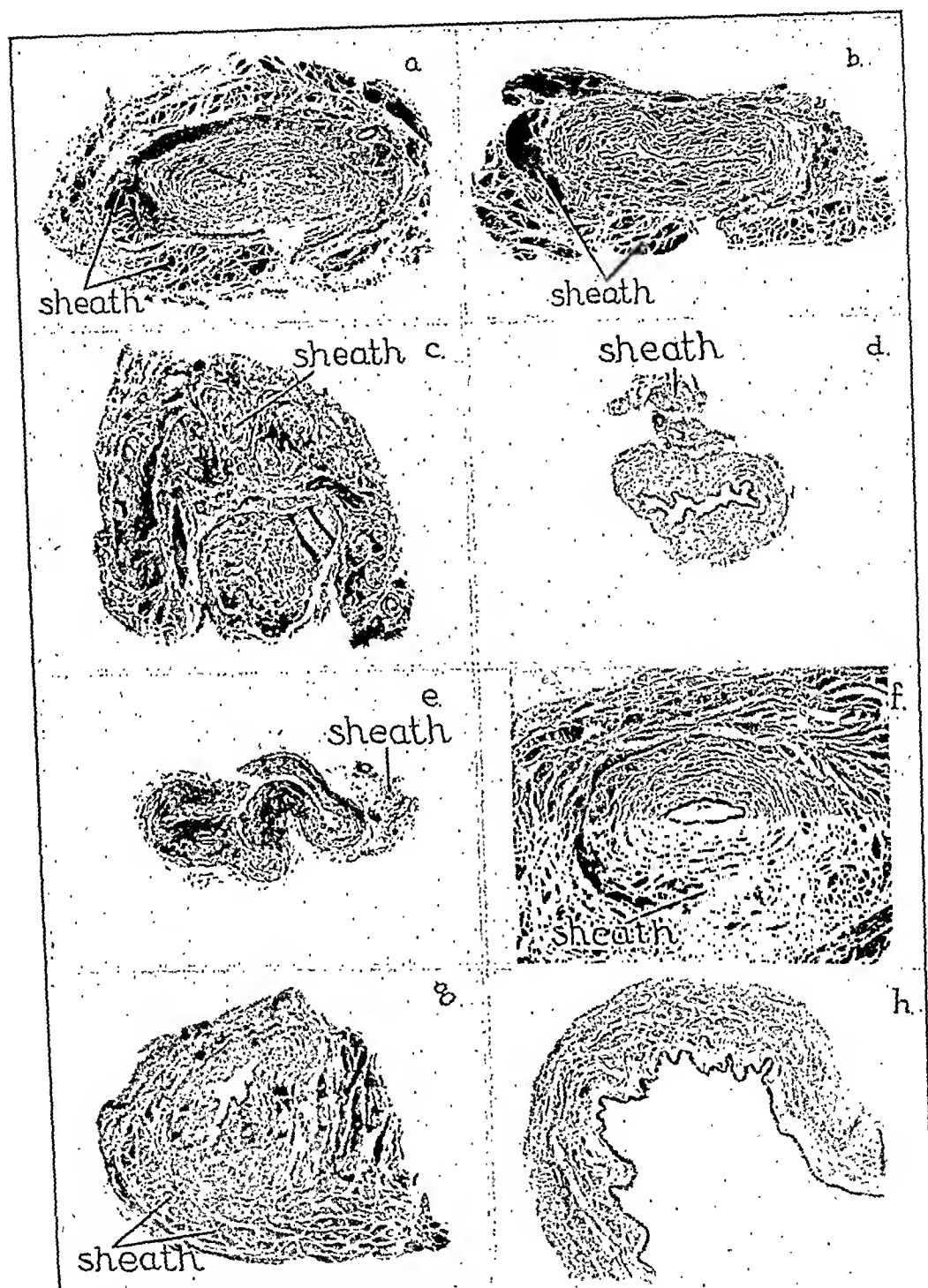


Fig. 4.—a, Pregnant ureter, left, at bladder, showing hypertrophy of the sheath of Waldeyer ( $\times 15$ ).  
 b, Pregnant ureter, right, at bladder, same patient as a, showing hypertrophy of the sheath of Waldeyer ( $\times 15$ ).  
 c, Another type of hypertrophied sheath of Waldeyer, associated with pregnancy ( $\times 15$ ).  
 d and e, Different types of nonpregnant ureters, at bladder ( $\times 15$ ).  
 f, Intramural portion of pregnant ureter, showing that sheath does not arise from bladder musculature ( $\times 35$ ).  
 g, Hypertrophic sheath of ureter at bladder in patient with ectopic pregnancy of seven weeks' duration ( $\times 15$ ).  
 h, Pregnant ureter, mild abdominal spindle, 17 mm. in diameter ( $\times 35$ ).

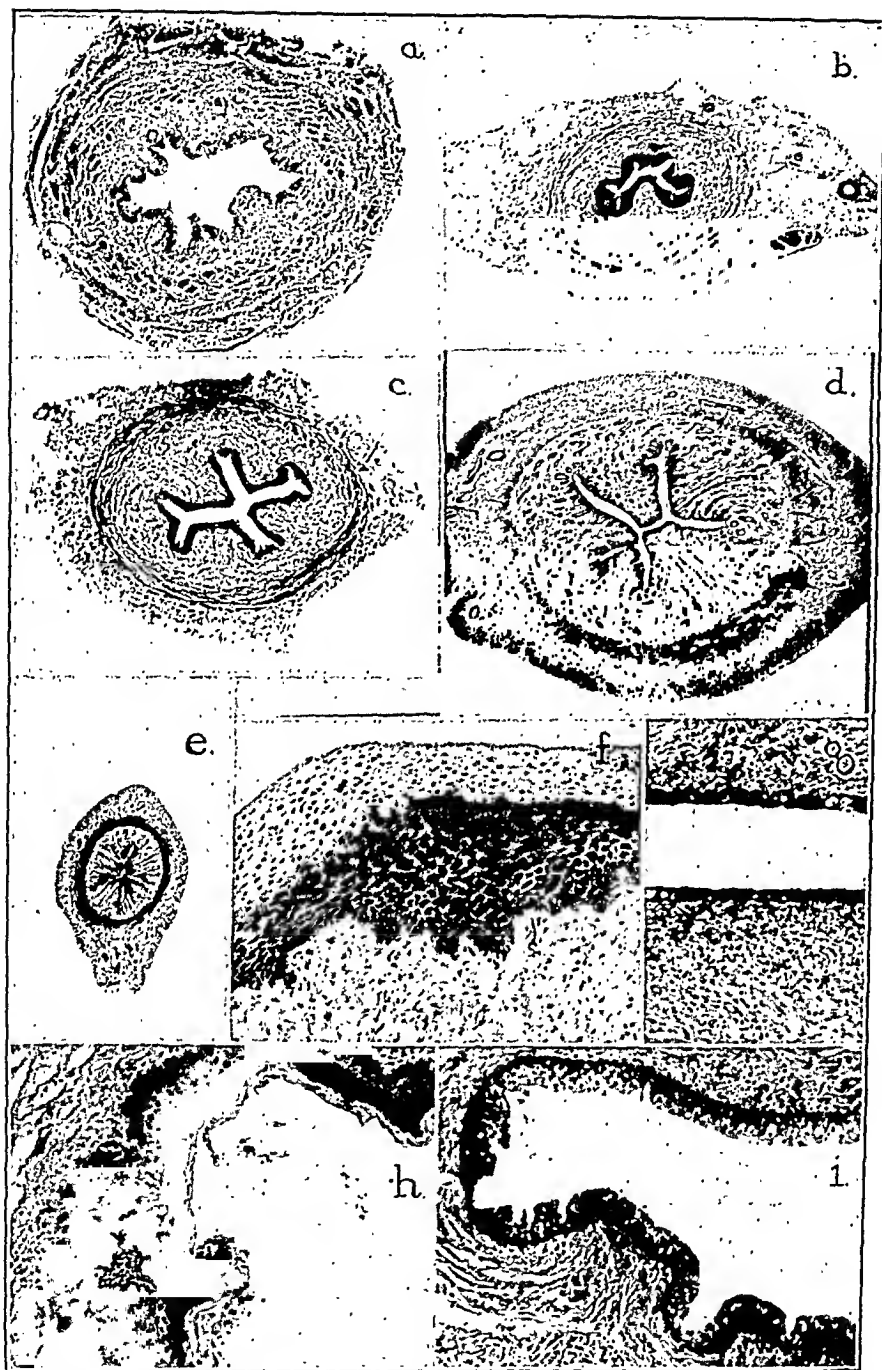


Fig. 5.—*a*, Nonpregnant ureter, midabdominal spindle. Note compact wall, high mucosa and no dilatation ( $\times 35$ ).

*b*, Section of juxtavesical portion of dog's ureter, animal having been castrated and injected with amniotin. No definite change noted when compared with control ( $\times 15$ ).

*c*, Control ureter ( $\times 15$ ).

*d*, Uterine horn of castrated dog primed with amniotin ( $\times 15$ ).

*e*, Uterine horn, control ( $\times 15$ ).

*f*, Vagina of castrated primed dog showing marked growth effect ( $\times 140$ ).

*g*, Vagina of control dog ( $\times 140$ ).

*h*, Urethra of castrated, primed dog, showing mucosa changed to a squamous cell type with cornification ( $\times 140$ ).

*i*, Urethra of control dog ( $\times 140$ ).

bladder, is 17 mm., dilatation beginning at the brim of the pelvis. The wall of the ureter is thinned out; the mucosa is normal but quite low and there is some hypertrophy of the circular layer of musculature. The internal and external layers are seen but are not well developed. There is a good deal of edema present which separates the muscle bundles and also loosens the connective tissue fibers. In the wall of the abdominal portion of all of the pregnant ureters studied, there were found small collections of round cells, mostly confined to the tunica propria or adventitia. It was difficult to study mucosal changes for many of the sections showed autolysis and desquamation of the epithelial cells; and then, with dilatation of the lumen, the mucosa becomes very low, being only 2 to 3 cells high.

Fig. 5, *a* shows a fairly high magnification of a normal nonpregnant ureter in its midabdominal portion. The absence of muscular hypertrophy, edema and vascularity is to be noted. The circular layer comprises the major portion of the muscular wall.

Wishing to observe the dilatation changes occurring in the ureter when not associated with pregnancy, we were able to obtain hydroureters produced by metastatic parametrial masses from a carcinoma of the cervix. It was definitely shown that the dilatation changes were due to pressure exerted by the growing metastatic tumor in the parametrium. Microscopic examination of the intramural and juxtavesical portions of the ureter showed no evidence of obstruction at this location, although epidermoid carcinoma was seen surrounding the wall of the ureter. The section of the dilated ureter taken just above the brim of the pelvis showed edema of the wall which separated the hypertrophied muscle bundles one from another. Here, as in the pregnant ureters, the circular layer comprised the major portion of the muscular wall. In this case, the hypertrophy is produced by the increasing muscular effort of the ureter in its endeavor to expel urine through its partially obstructed lumen. This is an example of work hypertrophy.

During the investigation of the urinary tract with pregnancy, the examination of the trigone revealed definite hypertrophy of the muscle layers associated with edema and increased vascularity. It was difficult to definitely determine if hypertrophic changes also occurred in the bladder, as the size of the muscle bundles vary greatly, depending on the bladder being contracted or distended. However, we believe that hypertrophy of the musculature does take place.

At this point, we wish to make a few remarks in regard to the cystoscopic findings during pregnancy. We find that the most satisfactory method of cystoscopy in the presence of pregnancy is the Kelly method, in which the patient is in the genupectoral position, thus permitting an excellent view of the fully distended bladder, made possible by

the dropping away of the enlarged uterus. The urethra is found to be soft, vascular, and quite easily dilatable. The bladder mucosa at the base is usually slightly hyperemic, while the trigone gives an even more injected appearance. It is frequently said that the distance from the internal urinary meatus to the ureteral orifice is increased, as is also the length of the interureteric ridge. One is impressed by the fact that the orifices always seem much higher up in the bladder and more laterally displaced during pregnancy. However, actual measurements, compared to the controls, showed no increase in the size of the trigone. It is probable that the urethra is somewhat elongated by the growing uterus, which would account for the apparent change.

Another observation of interest which we frequently have found is that when a catheter, armed with a 4 mm. wax bulb, is introduced up the ureter during the latter months of pregnancy, obstruction is met with at the brim of the pelvis, and on withdrawal, there is considerable "hang" encountered at this same point. However, if this procedure is carried out shortly after delivery, the obstruction and "hang" have completely disappeared. This would indicate that whatever obstruction had been present during pregnancy has now been removed by the birth of the child. It would seem that these observations would support the theory of pressure as the etiologic factor in the production of dilatation.

Carson, in his autopsy study of ureteral dilatation of pregnancy in sixteen cases, found constant dilatation of the right ureter with changes in the left nearly as frequent. He states that pressure against the ureter produces dilatation and with the introduction of pyogenic organisms, an inflammatory reaction may develop, with the formation of scar tissue and resulting stricture. One of the three patients, in whom he found inflammatory strictures, I had treated for a severe pyelonephritis with no avail, necessitating the termination of the pregnancy at the thirty-fifth week. Unfortunately, the patient died and autopsy revealed a definite stricture, measuring 4 to 5 cm. in thickness, situated 6 cm. below the ureteropelvic junction.

Our histologic studies were made, as far as we could determine, on normal urinary systems, and as above mentioned, no evidence of stricture formation could be made out. Duncan and Seng, in their series of 156 ureters studied, stated that one stricture of the ureter was found.

Dugald Baird, in an exhaustive autopsy study of the ureters in 102 women during pregnancy or within a few days following delivery, found ureteral dilatation of very common occurrence, 85 per cent in the right urinary tract and 72 per cent in the left. He confirms the observation first made by Hofbauer concerning the hypertrophy of the ureteral sheath during pregnancy, and he is of the opinion, from studies made on the living at the time of cesarean section and on undelivered women at autopsy, that the ureter can be compressed between the uterus and psoas muscle on the right side. We have also observed at autopsy how readily the exposed right ureter at the pelvic brim can be compressed by the enlarged uterus, and we feel that this is a causative factor in the production of dilatation.

## 6. OBSERVATIONS ON THE URINARY TRACT OF SPAYED DOGS, BEING SUBJECTED TO PROLONGED INJECTIONS OF AMNIOTIN

From a survey of the literature and the differences of opinion that exist as to the etiology of ureteral dilatation, it is evident that the question is complex and that several factors may play a rôle in its production.

From our study of the urinary tract in pregnancy, we find that dilatation changes occur as early as the fifteenth week when the growing uterus is rising out of the pelvis. The ureter soon becomes dilated, tortuous, and sacculated, and there is a decrease in its rhythmical expulsive force due to loss of tone. This atony affects the entire ureter with the exception of its lower portion where it is reinforced by the ureteral sheath. The examination of the ureter in the patient dying following the ectopic pregnancy of seven weeks' duration showed definite hypertrophic changes of the ureteral sheath, as well as an increased vascularity, softening and atony of the abdominal ureter. It is this preliminary atonic change which allows the soft, pregnant uterus to compress the ureteral wall, with a resulting dilatation. The degree of dilatation and tortuosity is not nearly so marked in the presence of an impacted, dense fibroid of years' duration. These atonic and hypertrophic manifestations must be the result of hormonal activity elaborated by the process of pregnancy.

When one considers that the generative and urinary systems arise embryologically from the same anlage, and that the ureter is a budding off from the wolffian duct, it is not too speculative to deduce that the same hormones, incidental to pregnancy, which produce gestational changes, would also affect the urinary system. We know that during the progress of pregnancy, large quantities of anterior pituitary sex hormone and estrin are found in the urine. The luteinizing substance designated as prolan by Zondek and Aschheim, reaches its maximum excretion of 5,000 to 6,000 M. U. per liter of urine during the fifth month of pregnancy; whereas, the excretion of estrin in the urine during early pregnancy is quite low, and ascends to its maximum of 10,000 to 40,000 M. U. per liter in the last month of gestation. Following delivery, there is a precipitous fall in the quantity of estrin excreted, which is due to the loss of its main source of supply, the placenta. Iscovesco, in 1912, showed that this organ contains large quantities of this growth substance, and now, estrin for therapeutic use is largely obtained from the placenta and amniotic fluid of cattle. As prolan is free of the growth promoting hormone, and as estrin is capable of producing growth, vascularity and edema in the generative tract of a spayed mouse, it is possible that this growth producing substance, estrin, is directly responsible for the muscular hypertrophy and vascularity in the trigone, bladder and ureter.

With the termination of pregnancy, the regressive changes in the urinary tract seem to go hand in hand with those occurring in the generative system.

Mengert has investigated the effect of pregnancy upon the ureters of common animals, using forty-two mammals of eight species, half of which were pregnant and the others being used as controls. The series examined included the cow, macacus monkey, dog, cat, rabbit, guinea pig, hog, and rat. In brief, a summary of his findings is as follows: There was no dilatation of the ureter found in any of the pregnant animals examined. A significant increase in the proportionate area of the ureteral sheath was noted in the monkey and the cow, and a significant decrease in the rabbit. The ureteral sheath does not seem to follow any set rule with regard to pregnancy. There was no significant hypertrophy of the circular musculature and the mucosa did not show any increase in the number of cell layers or in the size of the individual cell elements. He concludes from his observations that pregnancy has no effect upon the ureters of the animals studied.

On reviewing his work on the average area of circular musculature of the juxta-vesical portion of the ureter of the different pregnant and nonpregnant animals, it was noted that only the dog, monkey, and hog showed an increased area of musculature during pregnancy; and only in the dog did the change seem significant. Mengert felt that this change lost its significance when it was observed that the pregnant animal weighed twice as much as the control.

In view of this finding, we thought it would be of interest to see what changes, if any, would occur in the urinary tract of a spayed dog after prolonged injections of amniotin. The following investigation was then undertaken.

Six healthy, medium-sized female dogs were selected, two of which were castrated, and on one an exploratory laparotomy was done to definitely rule out pregnancy; the ovaries were not disturbed. These three animals received daily injections of amniotin in oil,\* until each had received a total of 5,250 R. U.; the daily dose being 100 units. For each of these injected animals there was a control, two being castrated and the remaining one was a normal control for the noncastrated injected animal. The injections were begun on February 18, and eighteen days later, bleeding from the vagina began. This was noted in the two castrated dogs; however, the remaining one which had not been castrated did not show bleeding until eight days later. We had contemplated giving the amniotin over a period of seventy days, which is approximately the time of gestation in dogs; however, distemper broke out in the kennel, so on the fifty-third day we decided to end the experiment before the animals became seriously affected. The dogs were then autopsied.

The gross description of the genitourinary organs follows: The uterus and vagina of the injected animals showed, as was expected, marked enlargement when compared to the castrated controls. The length of the vagina was not changed by the hormone but there was a marked thickening of the wall, 8 mm. as compared to 3 mm. There was no variation in the length of the ureters and there was no marked change in their diameters. The ureters were carefully measured at the bladder, in the midabdominal portion and at the ureteropelvic junction. The average variation of the diameters was between 1 and 1.5 mm. The diameters of the castrated controls measured 2 to 2.5 mm., whereas the animals that were castrated and injected measured 3 to 3.5 mm.

\*Supplied through the courtesy of E. R. Squibb and Sons.



*Microscopic Findings.*—There was no significant variation in size or structure found between the ureter of the stimulated dog and its control. There was no apparent change in the musculature or in the connective tissue. The mucosa was of the transitional type and showed no evidence of a change to squamous epithelium. Several of the dogs showed clumps of lymphocytes in the submucosa. None of the sections showed definite dilatation of the lumen. Fig. 5, *b* shows ureter of castrated injected dog at the bladder. Fig. 5, *c* shows ureter of castrated control at the same level. The ureter of the control is definitely larger than that of the injected castrated dog. This finding loses its significance when we realize that the control dog weighed ten pounds more than the injected animal. The uteri of the three castrated animals which received the hormone showed similar hypertrophic change. The uterine walls were much thicker, due to the increase in size of the muscle layers and the individual muscle fibers. Fig. 5, *d* shows section of uterine horn of castrated injected dog. Fig. 5, *e* shows section of uterine horn of castrated control. However, the most striking change was in the endometrium. This structure showed great thickening, vascularity, and loosening of the stroma. The main change was seen in the glands, which were longer, more dilated, and slightly tortuous. No evidence of secretion was made out. The epithelial cells lining the glands were of the high columnar type with the nuclei occupying the basal position. The uterine changes in the noncastrated injected dog showed hypertrophic changes but not so marked as in the ones just described. The uteri of the castrated controls were very small and atrophic, the stroma compact, and the mucosa very low.

The vagina of the stimulated, spayed dog showed the usual changes of estrus, the mucosa consisting of a thick layer of stratified squamous epithelium. The superficial half was composed of pale staining cornified cells; in the deeper portion, dark blue staining epithelial cells, which grew downward in numerous papillae, were seen. The wall of the vagina showed marked proliferative changes when compared to that of the control (see Fig. 5, *f* and *g*, for comparison).

In the routine examination of the organs, there was noted a marked change in the urethral mucosa. This structure normally shows transitional epithelium, the surface cells being cuboidal in type. However, the mucosa of the castrated dogs that received the hormone was changed into a typical stratified epithelium. The mucosa was definitely thickened and its superficial portion consisted of pale staining, cornified epithelial cells, similar to those seen in the primed vagina. The basal portion consisted of deep blue staining cells with papillary downgrowths. The muscle bundles showed no evidence of hypertrophy (see Fig. 5, *h* and *i*). The urethral section of the castrated control showed the usual low transitional type of epithelium.

In summarizing the results obtained from this short study, we find the following: There was no significant change observed in the ureters of the castrated injected animals as compared to the castrated controls. A marked growth of the uterus and vagina was obtained with definite hyperplasia of the endometrium and cornification of the superficial vaginal epithelium. In the urethra of the stimulated animals, the transitional epithelium was changed to a definite stratified type with cornification of the surface epithelium.

These investigations will be continued, for it is impossible to draw any definite conclusions based on such a small series of observations.

#### ETIOLOGY OF URETERAL DILATATION

We have shown by this investigation that some degree of dilatation of the urinary tract occurs with every pregnancy. The right side is



affected much more frequently than the left, and the dilatation invariably begins at the brim of the pelvis.

The cause of this dilatation is dependent upon two primary factors, namely, first, a softening process in the ureter due to hormonal activity, and second, pressure exerted by the growing uterus upon the ureter at the brim of the pelvis.

We have seen that early in pregnancy certain changes in the urinary tract become evident. The wall of the abdominal ureter becomes softer, flaccid, and atonic. Associated with this softening process, hypertrophic changes become noticeable throughout the ureter. The most striking change was noted in its lower end, where there was marked hypertrophy of the ureteral sheath of Waldeyer. The rest of the ureter also participates in this hypertrophic development but not to such a marked degree. The circular musculature of the abdominal spindle was the most involved. We have seen that at the seventh week of pregnancy, definite hypertrophic changes are present in the juxtavesical portion of the ureter, associated with increased edema and vascularity.

When we consider that the generative and urinary systems arise embryologically from the same anlage, it does not seem too hypothetical to reason that the hormones elaborated during pregnancy might have some effect upon the urinary system. It would seem most logical to deduce that estrin, which is elaborated in enormous quantities during pregnancy and produces vascularity, edema, hypertrophy, and swelling of the generative tract, could produce a similar change in the urinary tract.

In support of our hypothesis of hormonal activity upon the ureter, we present this very interesting case. We were fortunate in obtaining the urinary tract of a patient dying from a tumor of the testicle with generalized metastasis. The following is a description of one of the metastatic masses occurring in a lymph node. There are seen many tumor masses separated by fibrous tissue bands, into which, in several areas, fresh hemorrhage has occurred. In some areas the tumor is necrotic. In its well-preserved portions it consists of cells which resemble epithelial cells. The nuclei are irregular in size and shape and vary in intensity of staining. The cytoplasm is drawn out into long strands which interlace and surround small spaces. There are numerous masses of pink-staining material which vary in size and are undoubtedly synechium. Imbedded in them are numbers of Langhans cells with irregular, very deep staining nuclei which vary greatly in size and shape, but are usually ovoid in form. The diagnosis of chorionepithelioma was made (see Fig. 6, *a*). In the testicle removed at operation, no definite chorionic epithelium was seen; however, the urine was strongly positive for prolan on two occasions. The examination of the ureter showed definite hypertrophic changes throughout the whole ureter but was most marked in the juxtavesical portion. Here, there was tremendous hypertrophy of the sheath

of Waldeyer, the greatest external diameter measuring 8 mm. There was general muscular hypertrophy seen throughout the ureter and the mucosa was also thickened, the superficial cells being slightly flattened. There was no evidence of any dilatation of the urinary tract. As we have already mentioned, Hofbauer is of the opinion that hypertrophy of the ureteral sheath is the important factor in the production of dilatation in the ureter. However, this observation does not support his views (see Fig. 6, b).

It is interesting to speculate why the marked hypertrophic changes occurred in the ureter when associated with the chorionepithelioma. It is known that with the hydatidiform moles and chorionepithelioma there is a great outpouring of prolan in the urine, which produces changes in the vaginal epithelium of the test animal by indirect action through the ovary. This urine when injected into infantile mice causes maturation of the follicles with the production of estrin and a resulting cornification of the vaginal epithelium (estrus); hemorrhage into the enlarged

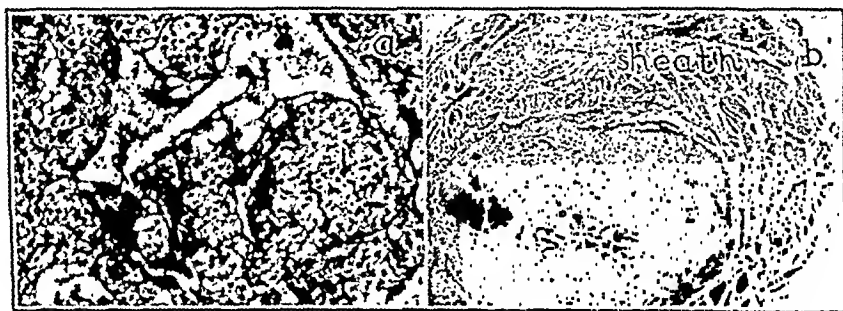


Fig. 6.—*a*. Chorionepithelioma in a man, the primary focus being a teratoma of the testicle ( $\times 140$ ).

*b*. Section of juxtavesical portion of ureter from man with chorionepithelioma, showing hypertrophy of the sheath of Waldeyer even more marked than that seen in pregnancy ( $\times 15$ ).

follicles and the formation of corpora lutea of normal appearance; also corpora lutea atretica, characterized by imbedment of the ovum in the lutein tissue (Zondek). It is thought that prolan is free of growth promoting hormone, so in order to explain the hypertrophic changes in the ureter, it would be most logical to deduce that this same indirect action occurred in the patient with the testicular tumor. The prolan elaborated by the trophoblastic tissue of the chorionepithelioma stimulated the testicle with a subsequent outpouring of growth hormone, which in turn produced hypertrophic changes in the ureter.

Having shown that the primary changes in the ureter are hormonal in action, we will now consider the subject of pressure, which is the second etiologic factor in the causation of dilatation.

In early pregnancy, when the uterus is confined to the pelvic bowl, the lower ends of the ureters show lateral displacement, but dilatation of this portion is rarely seen. At the fifteenth to sixteenth week of gestation, the growing uterus, rising out of the pelvis, may now exert

pressure upon the ureter at the pelvic brim. We have shown that a softening process of the ureter takes place with advancing pregnancy. This is of the greatest importance, for without this change, the soft semi-cystic uterus could not exert sufficient pressure on the unchanged ureter to cause its compression. The right ureter is more affected than the left for several reasons. The left ureter is protected and cushioned by the overlying sigmoid flexure, which also is a causative factor in the production of dextrorotation of the uterus. Baird has called attention to the fact that the right ureter is more exposed than the left, due to its anatomical course, and therefore is more easily compressed. Fig. 7 shows the right ureter crossing the iliac vessels at nearly a right angle; whereas, the left ureter, which is double, runs almost parallel to the

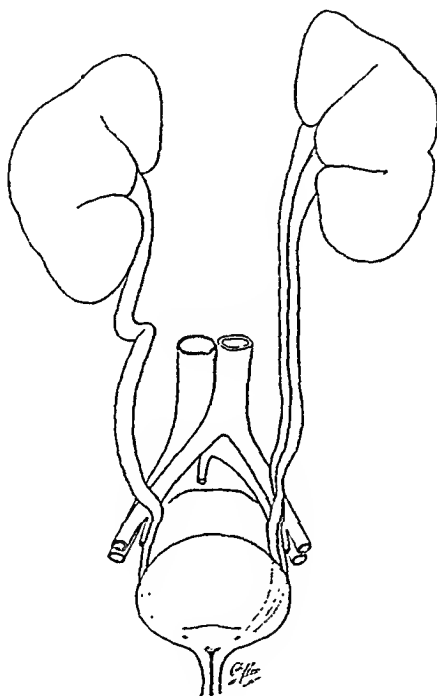


Fig. 7.—Autopsy drawing of urinary tract, patient dying at term. Note right ureter crossing iliac vessels at nearly a right angle, thus making it prominent and more susceptible to pressure than the left ureter, which runs nearly parallel to the iliac vessels.

vessels. This drawing which was made at autopsy, patient dying at term, shows that the dilatation of the abdominal ureter begins at the brim of the pelvis with kinking of its upper portion. The left double ureter is straight and is not dilated; its two portions join at the juxta-vesical region and enter the bladder as a single tube with one orifice. The pelvic ureters are not dilated.

One of us (J. M. H.) on several occasions, at operation and autopsy, has observed the markedly compressed ureter at the pelvic brim, produced by the overlying uterus.

We have been able to show definite regression of the ureteral and pelvic dilatations during pregnancy by the use of the indwelling catheter.

It is necessary for the continuous drainage to be maintained for at least forty-eight hours before decrease in capacity is noted. Even with continuous drainage, the decrease in dilatation would not be expected to be so very rapid for the ureter is still atonic and soft, due to the continuous action of estrin.

It has also been demonstrated that large uterine fibroids which fit the pelvis and impinge against the ureters at the pelvic brim produce upper tract dilatations. It is noticed that dilatation changes are not so marked even though some of the tumors have been present for several years. One might expect the dilatations to be more marked due to the greater density and the more prolonged pressure of the fibroma; however, this lack of increased dilatation is probably explained by the nonpregnant ureter being firmer and more compact, and therefore better able to withstand the compression.

Another point to support the theory of pressure is, that in catheterizing the right ureter during the latter part of pregnancy, using a catheter armed with a No. 4 mm. wax bulb, definite obstruction and "hang" are met with at the pelvic brim. When this same procedure is done following delivery, no obstruction or "hang" is encountered, showing that whatever obstruction existed during pregnancy was relieved by the birth of the child.

We are indebted to Dr. Hugh Spencer and his associates, in the Department of Pathology of the University of Maryland, for their cooperation and advice.

We wish to thank Dr. Carl Hartman, of the Department of Embryology of the Carnegie Institution of Washington, for his helpful suggestions.

We also wish to thank Mr. Carl Clarke and Mr. James Dunlop, of the Art Department of the University of Maryland, for these excellent illustrations, and also Miss Evelyn Glidden, of the Art Department of the Johns Hopkins Medical School, for her fine autopsy drawing of the urinary tract.

#### REFERENCES

- Rayer, Pierre: *Traite Maladies des Reins* 3: 1841. Cruveilhier: *Descriptive Anatomy*, pp. 585, 586, 1843. Kretschmer and Heaney: *J. A. M. A.* 85: 406, 1935. Kretschmer, Heaney, and Ockuly: *J. A. M. A.* 101: 2025, 1933. Duncan and Scng: *AM. J. OBST. & GYNEC.* 16: 557, 1928. Hofbauer: *Bull. Johns Hopkins Hosp.* 42: 118, 1928; *J. Urol.* 20: 413, 1928. Menees, Miller, and Holly: *Am. J. Roentgenol.* 24: 363, 1930. Kerr and Mackay: *Edinburgh M. J.* 40: 1933. Ude, Weum, and Urner: *Am. J. Roentgenol.* 31: 230, 1934. Lee and Mengert: *J. A. M. A.* 102: 102, 1934. Baker and Lewis: *J. A. M. A.* 104: 812, 1935. Bardeleben: *Handbuch der Anatomie des Menschen* 7: Part 1, 1902. Carson: *J. Urol.* 16: 167, 1926. Baird, Dugald: *Lancet* 2: 983, 1932. Mengert: *AM. J. OBST. & GYNEC.* 27: 544, 1934. Carreras, F., Faixat, F., and Figueras, I.: *Rev. españ. de obst. y ginec.* 16: 661, 1931. Friedl, F.: *Centralbl. f. Gynäk.* 57: 327, 1933. Mandruzzato, P.: *Ann. di ostet.* 53: 547, 1931. Jung: *Arch. f. Gynäk.* 144: 578, 1931. Scng, Magnus: *J. Urol.* 21: 475, 1929.

## THE HISTOGENESIS OF CERTAIN OVARIAN TUMORS AND THEIR BIOLOGIC EFFECTS\*

SAMUEL H. GEIST, M.D., NEW YORK, N. Y.

(From the Laboratories and Gynecological Service, Mount Sinai Hospital)

THE recent advances in our knowledge of ovarian neoplasms have in great part been based on a better understanding of the embryologic development of the gonad and of the biologic activity of that organ. Unfortunately both of these important concepts in the life history of the ovary are still in a state of flux.

Early in the development of the gonad, the surface epithelium of the *anlage* of the ovary becomes many layered and extends downward into the mesenchyme as solid cell cords. This represents the indifferent gonadal stage. This stage rapidly passes into that of the definitive sex gland. The character and fate of the cell cords from the surface epithelium depend on the type of gonad (male or female) that develops.

In the male the cell cords form the tubular system and possibly the interstitial cells, while in the female they become the undeveloped granulosa and theca interna cells, which later are utilized in the development of the graafian follicle. FischeI, and more recently Schiller, believe that these granulosa cell forerunners and the theca cell forerunners, as well as the interstitial cells of the testis, are derived not from the surface epithelium but from the mesenchyme. The weight of evidence at present, however, favors the coelomic epithelial origin.

In addition to the two-cell types mentioned, there remain in the female gonad remnants of structures that achieve full development only in the male. The structures we identify as cords and tubules in the region of the "rete ovarii." These structures presumably remain quiescent, but may, under proper but as yet undetermined stimulation, develop and functionate in a male direction.

Occasionally gonads are encountered, that are functionally inefficient, the improperly descended gonad (the cryptorchid), the sex glands of the hermaphrodite, or the gonads of hosts that are somatically inferior, as individuals with infantile genitalia and sterility. In these latter cases some of the cells of the original epithelial invasion remain, which not only are functionless, but which do not at any time have the potentiality for developing along male lines as do the rete structures, or along female lines as do the granulosa or theca forerunners.

It is important to keep these embryologic possibilities in mind, for it is this concept that enables us to attempt to classify some tumors histogenetically.

---

\*Presented at a meeting of the New York Obstetrical Society, March 12, 1935.

The ovary has been found to produce at least two definite hormones. One, the estrogenic factor, is apparently developed by the granulosa cells as shown by Frank and the theca cells as proved by Zondek. The second, "progestin," is derived from the corpus luteum as demonstrated by Corner and others. The estrogenic hormone is presumably active in some tumors.

We know that the tumors of various ductless glands give rise to clinical signs and symptoms suggestive of a perverted or exaggerated physiologic activity of the tumor or of the gland itself, as for example, the tumor of the pituitary, thyroid, adrenal, pineal and the gland under discussion, the ovary.

Four tumor types in the ovary may be recognized as distinct entities, and have been classified, because of the belief that one can identify their site of origin, and can also associate with them definite effects which may be recognized clinically.

These groups are: (1) The granulosa cell tumor; (2) the theca interna cell tumor; (3) the arrhenoblastoma, or rete cell tumor; and (4) the dysgerminoma, or indifferent cell tumor.

#### THE GRANULOSA CELL TUMOR

A group of tumors containing ovalike inclusions were described by Acconci, Emanuel, Amann, Blau, and others. Lippman showed that these inclusions were not ova but cell secretion. Schiminicke pointed out the similarity between the radial arrangement of the cells of these tumors and that of the granulosa cells in the follicles. Many names were suggested by various authors, depending on their interpretation of the origin, or the histologic make-up of these neoplasms. Robert Meyer suggested the persistent primitive granulosa cell balls as the site of origin and the name granulosa cell tumor was then advanced by V. Werdt.

As was mentioned earlier in this paper when discussing the embryology, the surface cell invasion into the underlying mesenchyme probably results in the formation of the active parenchyma of the ovary, and it is from some of these cells, the unused forerunners of the granulosa cells, I believe the granulosa cell tumors arise. The granulosa cell balls have already reached a definite stage of development and would hardly be expected to produce such bizarre tumors as will be described. The undifferentiated forerunner, probably under an as yet unknown stimulus, has a far greater potentiality for variation.

These tumors are usually unilateral. They occur as bilateral tumors in about 10 per cent of the cases (Szatlmay). They vary in size from small 6 by 5 mm. tumors (Schiller) (Fig. 1) to masses twice the size of an adult head (Dworzak) (Fig. 2). The surface is encapsulated, usually smooth, with varying sized bosses. As a rule they are soft, mainly solid masses, though cysts may be present, either single or multiple, large or small. The tumor is sessile, but rarely may be pedunculated and thus may undergo torsion.

On section the growth is a medullary, cellular, yellowish tumor. Connective tissue bundles traverse the cut surface irregularly, giving a finely or coarsely lobulated appearance to the cut surface. When cysts are present, their inner wall may be smooth or shaggy, and the contents vary in color and consistency, at times being a thin, yellowish or pinkish fluid, and at others, a thick mucinous or gelatinous grayish white opaque substance.

Hemorrhage may take place into the tumor tissue or even into the cysts, and necrosis of varying extent is not uncommon (Fig. 3).

The histologic picture varies tremendously, though, in the main, three types may be differentiated, the folliculoid, the cylindroid, and the mixed type. The connective tissue arrangement and distribution plays a great rôle in determining the type (Robert Meyer).



Fig. 1.—Small tumor contained in ovary (Goldberger's case). Gross (cylindroid type).



Fig. 2.—Large tumor. Atypical type.

At times in the same tumor all three types of structure may be found and not infrequently only the careful study of many areas will enable one to identify the neoplasm definitely as a granulosa cell tumor.

The folliculoid type, which is the most striking, presents a most unusual picture. (Fig. 4.) The cells are polygonal or round, moderate sized, closely packed, with a central vesicular nucleus, resembling the granulosa cells of the young developing follicle. They form larger and smaller compact cell masses, showing in some instances mitoses, and are surrounded by connective tissue bundles. Fat stains demon-

strate the existence of small amounts of lipid in these cells, but apparently a greater amount in the connective tissue (Schiller).

In the solid masses one finds small cavities, in places resembling follicles. They are usually round, but may become confluent and give rise to irregularly shaped large-sized cavities. In these cavities, round or oval structures are found, sometimes representing degenerating cells or colloid material or cell secretion. At times a single



Fig. 3.—Lobulated tumor. Folliculoid type.

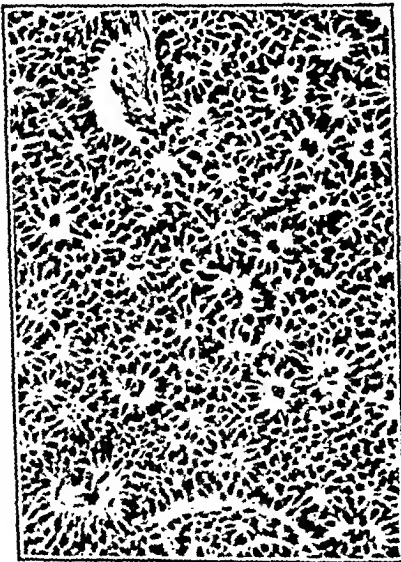


Fig. 4.

Fig. 4.—Folliculoid type. Solid cell nests with ovalike structures.



Fig. 5.

Fig. 5.—Cylindroid type. Solid cell columns separated by connective tissue.

swollen degenerating cell fills the cavity and has been mistaken for an ovum. The cells surrounding the cavity are often radially arranged, and at the periphery of the cell mass where it abuts the connective tissue, the same radial arrangement is present. While this arrangement suggests the follicular origin, it has been shown by Schiminicke to be just an arrangement trait of the tumor cells.

At the periphery and in the substance of the cell masses vacuoles of varying size are found, the so-called Call-Exner bodies, the significance and origin of which are



not known. Similar bodies appear in normal structures, as the granulosa layer and other neoplasms (Schiller). The connective tissue may invade the solid cell masses, subdividing them into small groups. The tumor cells may at times take on a more spindle type, resembling the connective tissue cell.

The cylindroid form is composed of epithelial cells, cuboidal or spindle in type, separated by fine connective tissue bundles. Here, too, spaces are found that may be empty or contain remains of cells or connective tissue. The cell columns may have bizarre shapes, due to the ingrowth and pressure of the connective tissue (Fig. 5). The connective tissue may become hyaline, or remain finely fibrillar. It may even separate individual cells from each other by ingrowths of fine fibers or so demarcate the cell column as to give a picture of wavy pattern, the so-called *moiré* type.

One often finds a combination of the folliculoid and cylindromatous types, and not infrequently a sarcomatous form, in which it is necessary to make careful studies to identify the true nature of the growth. This latter type is composed of spindle (Fig. 6) or polymorphous cells that intermix with no definite arrangement. Here and there one finds more epithelial-like cell groups, and some definite areas that are typically granulosa cell in type. The cells are separated into large groups by con-

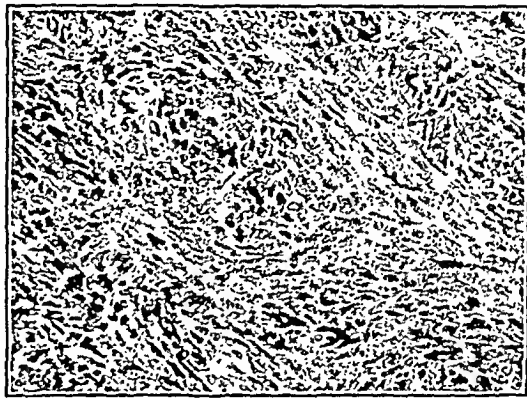


Fig. 6.—Sarcoma-like tumor.

nective tissue bundles containing vessels, and this lobular structure may even be noted grossly. In some areas tubular structures are found, and rosettes of tumor cells may occur to further complicate the picture. At times adenomatous areas are found, or small round tubules with rather slender high cuboidal epithelium and no evidence of a follicular type.

Primarily the tumors are solid but they may undergo degenerative changes due to circulatory disturbances. Areas of hemorrhage, necrosis, and cyst formation are not infrequently encountered. The cysts, both large and small, are the results of degeneration. Burg reported a case with 5 liters of fluid and a small solid portion only. The possibility of the cell secretion forming small spaces and later from pressure causing cell death must be kept in mind, for often the remains of cells, nuclear fragments and granular debris are found in these small follicle-like spaces. The radial arrangement of the border cells suggests a follicle, but this tendency is common in any growth process where degeneration takes place. The lining of the cysts when present is usually a low epithelium.

It is possible that the cell secretion contains the hormone which we now know is present in these tumors, and which, we believe, acts on the host to produce the distinctive clinical picture which so commonly is associated with granulosa cell tumors. Lipoid is present in these tumors. It is found in the cells, but more often and in

larger amounts in the connective tissue (Schiller). This is in contrast to the theca cell tumors as will be mentioned later, where the lipoid is found almost exclusively in the cellular islands.

R. Meyer, Neumann, Klaften, Siebke, Suschania, and Salmon found an estrogenic hormone in these tumors, but not in large amounts. Pahl, in a child of nine with a granulosa cell tumor, reports a positive Aschheim-Zondek test.

The granulosa cell tumors may occur at any age though the fourth and fifth decade is the most common. Klaften states that they occur before puberty in 8.9 per cent, during sexual activity in 48.7 per cent, and at or after the menopause in 42.5 per cent. He reported the case of a patient nine years of age with precocious puberty. After removal of the tumor the symptoms regressed. Novak reported cases at three, five, and six years, respectively, all with *pubertas precox*. Other authors also have reported cases in children (Szathmàry), all with atypical bleeding, with pubic and axillary hair, and adult-sized pelvic organs. In one case, a child, reported by Meyer, colostrum was present in the breasts. Bland and Goldstein detail a case with a positive estrin finding in the urine two days before operation, and negative seven days postoperative. This patient was seven years old with precocious sexual development.

The tumor may occur in very old women between seventy and eighty as reported by Schroeder, Isbruek, Neumann, Schiller, Schiffman and others, with or without atypical bleeding, but usually with a well-preserved uterus and hyperplastic endometrium.

The most striking distinctive symptom is irregular uterine bleeding, sometimes of long duration, and occasionally preceded by short periods of amenorrhea, or, as in a case of Plate, followed by amenorrhea. We recently had a case in a woman of thirty-six with a three-year period of amenorrhea, a resting endometrium and a small endometrial polyp associated with an atypical granulosa cell tumor with abundant estrogenic hormone in the tumor tissue (Salmon).

The uterus is usually soft, hyperemic and enlarged. The myometrium is hypertrophied and the endometrium is hyperplastic. Adenomatous polyps of the uterus are not infrequently encountered.

Habbe reports four cases in the climacteric with endometrial hyperplasia, but without a history of bleeding, while Schroeder mentions a case in a woman thirty-six, with menstrual irregularities and an atrophic mucosa.

Klaften has found glycogen in the hyperplastic mucosa when the hyperplasia was the result of tumor activity even in the climacteric.

Tietze has reported hypertrophy of the tubal epithelium.

The breasts are not infrequently enlarged, a fact that one attempts also to correlate with the tumor activity. This enlargement regresses with the removal of the tumor. Klaften has reported hirsutism which has not regressed with the ablation of the growth and is probably not related to the tumor. Bergstrand reports six cases with hirsutism. Klaften has reported an increase in the basal metabolic rate in one instance as high as plus 24, which returned to normal following removal of the neoplasm. Ascites is not common, though Szathmàry reports it in 10 per cent of the cases. Adhesions occur only late in the disease.

The tumors often present the histologic picture of malignant neoplasms, with cell atypism and mitoses, and at times infiltration. Schiller divides them into malignant and nonmalignant, stating however that the division is really clinical and not histologic.

They rarely recur and if they do, the recurrence is usually local. The removal of the second tumor may be followed by a permanent cure. Szathmàry reports 10 per cent of local recurrence, and 15 per cent in the opposite ovary.

The benign cases are usually unilateral and Schiller states that when unilateral they are practically always benign. The involvement of the second ovary may be

metastatic, secondary invasion or primary involvement. Schiller has suggested the term granulosa cell tumor for the benign, and granulosa cell carcinoma for the malignant.

Metastases are rare but occur not only locally, or in the other ovary, but also in the abdominal viscera and retroperitoneal lymph nodes. Soltman reports metastases in the bones; and Maresch, also. Granulosa cell tumors may arise in the retroperitoneal ovarian segments, and Stoltz states that in 69 per cent of supernumerary ovarian segments some type of tumor has been present in them.

Granulosa cell tumors when benign are easily treated by operative removal and the patient may and does remain well and physiologically normal. Pregnancy even has followed. In the malignant type, when a recurrence develops it may be benign (Schiller) or malignant in type. With the appearance of recurrence or metastasis, the typical clinical signs may reappear, to regress on subsequent removal of the growth. The prognosis is good. In 7.5 per cent of the cases, however (Klaften), they were inoperable.

A large number of patients with malignant cases have been treated with post-operative radiotherapy (Klaften, Plate, Schiffman, Habbe, Dworzak, Schulze) with good result.

These tumors have been investigated for their hormone content. As before mentioned, while it has been found by transplantation experiments, the estrogenic hormone has been isolated also by tumor extraction. In one of our cases Dr. Salmon has obtained one mouse unit per gram of tumor. Dworzak and Podleschka report a case with 50 m. u. per liter of urine in the intermenstruum. This, however, is not an unusual amount.

With the removal of the tumor the bleeding, breast enlargement, and uterine mucosal hyperplasia regress. With the appearance of a recurrence these symptoms again make their appearance, indicating the part played by the tumor tissue. These findings suggest that the clinical symptoms are due, at least in part, to the activity of the hormone.

It is evident that here we have a distinctive tumor, both histologically and clinically, whose cells produce a hormone that affects the normal physiology of the host, i.e., a tumor that has a genetic, morphologic and biologic resemblance to granulosa cells.

#### THECA CELL TUMORS

In 1932 Löffler and Pricel described a group of tumors, six in number, which because of their distinctive gross, histologic and clinical characteristics, they believed were derived from the theca cells, forerunners in the ovarian parenchyma. In 1934 they reported four additional cases.

The parenchymal cells, both granulosa and theca interna, have definite common characteristics: both store or form lipid and both produce or store an estrogenic hormone. Zondek showed that the theca interna cells contain an estrogenic hormone, usually in greater amount than in the granulosa cells. In addition both cell types stimulate the formation of connective tissue, which has a tendency to become hyalinized, though this is more marked in the theca cells. In addition, these latter cells may even produce fine connective tissue fibrils.

The theca cell tumors have all these characteristics coupled with a striking morphologic pattern, and nowhere showing areas suggestive of granulosa cell tumor, thus leading us to believe that they form a separate and distinct group. In addition, the distribution of the lipid in the theca cell tumors differs from that in the granulosa cell tumors. In the latter the lipid is found mainly in the connective tissue bundles (Schiller), while in the theca tumor the lipid is found almost entirely in the cell islands, and only as small droplets in the connective tissue or at its periphery.

Grossly the theca cell tumors are distinctly different from the granulosa cell growth. Furthermore, the consistency and appearance in many instances is that of a fibroma, whereas the granulosa cell tumor is a cellular, softer tumor. The hormone content also of the theca tumor in the one case examined was far greater in amount than that as yet reported in the granulosa cell tumor. Finally in all but two of the sixteen cases now recorded they occurred in women at or past the menopause.

Löffler and Priesel have reported in two publications ten cases, Melnik and Kantor have two additional cases, and we have had four cases of our own. (These latter cases will be reported in detail elsewhere.)

Grossly these tumors appear as hard, somewhat nodular tumors, which may reach the size of a child's head (Fig. 7). In one of our own cases it was represented by a large twisted cystic mass, the wall of which measured 2 cm. in thickness and was of a bright yellow color. The surface is smooth. It is hard except in the cystic type and suggests a fibroma grossly.



Fig. 7.—Fibroma-like tumor with small cellular areas (theca).

On section it has a striking appearance. The surface has a yellowish white color. On close inspection the tumor is seen to be composed of varying sized yellow islands separated by fine or coarser hyalinized connective tissue bundles (Fig. 7). Small hemorrhages may be present, and at times, cysts vary in size from pinhead to walnut. These may coalesce and form larger ones as in one of our cases. These cysts are degenerative in origin.

On the other hand, the cut section may present broad white glassy areas of connective tissue, with here and there, in these areas, tiny pinhead-sized islands of yellow color, and in addition, large isolated nodules of yellow tissue surrounded by the hyaline fibrous tissue (Fig. 8). Few blood vessels are present, except near the connective tissue capsule at the surface, and at the periphery of the fatty islands.

Histologically the tumors are very distinctive in structure. The yellow areas are composed of plump spindle cells or polygonal cells with central or at times excentric nuclei, dark staining and rich in chromatin. The cell protoplasm is vacuolated and contains fat (Fig. 9). The fat globules may also be present in the interstitial tissue to some extent, but only where cells still are present, and then usually as much smaller globules than in the cellular islands (Fig. 10). The epithelioid cells seem to have a tendency to be more numerous about the vessels.

The connective tissue bundles are hyaline to a great extent, and often large hyaline plaques are present in the midst of a cellular island (Fig. 11) with fine fibers extending out radially and surrounding the individual cells or seeming to enter them.



Fig. 8.

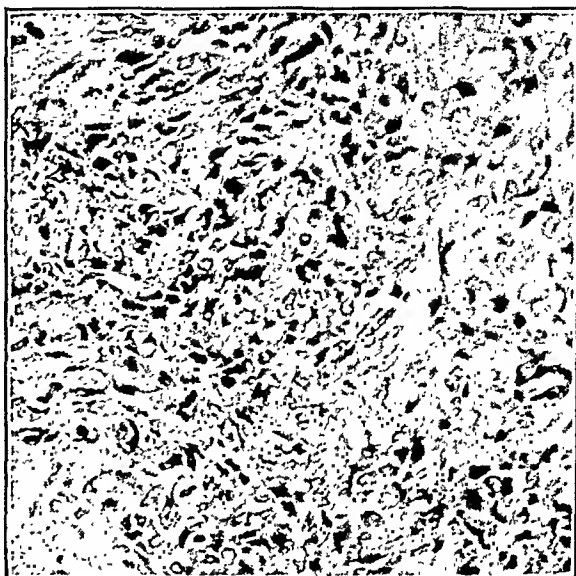


Fig. 9.

Fig. 8.—Hyaline type with well-demarcated cellular islands.

Fig. 9.—Cellular areas with vacuoles.



Fig. 10.



Fig. 11.

Fig. 10.—Fat in cellular areas, little in connective tissue areas.

Fig. 11.—Hyaline plaques with fibers radiating into cellular areas.

The fibrous tissue bundles vary in size, density, and structure. They may be very fine, composed of but a few fibrils, or so massive as to represent the greater part of the tumor as in one of our cases. They may be composed of few connective tissue bundles or large masses of hyaline tissue, and they may show many or few connective tissue cells with isolated, large, fat-containing cells in the meshes

of tissue. At the periphery of the hyaline plaques some fat droplets are present. Pigment granules, probably lipochrome, are found in some of the epithelioid cells, but mainly in the capillary endothelium. The cystic tumor previously mentioned had a 2 cm. thick wall composed of elements as above described.

The cysts when present may be smooth walled or shaggy. They contain a yellowish clear or turbid fluid and show no definite epithelial lining. Rarely a flattened endothelial-like lining is present in scattered areas.

Chemical analysis of the tumor shows it to contain a not unusual amount of lipid, but a relatively high content of cholesterol and cholesterol ester. The polaroscopic examination demonstrates that most of the fat is double refractile, and is in the cell islands.\*

The extraction of the tumor tissue also demonstrated that it contained a large amount of estrogenic hormone per gram. This fact helps to understand and explain some of the clinical symptoms and signs. In one case, already submitted for publication, in association with Spielman, we were able to demonstrate more than a mouse unit of estrogenic hormone per gram of tumor tissue.

The tumor is unilateral. In all the cases reported (sixteen) only two occurred in women before the menopause, one of Löffler and Priesel, at eighteen years, and one of ours, at twenty-one years of age.

Aside from the symptoms of any pelvic neoplasm of size, these tumors have certain definite and clear-cut symptoms. The most striking is atypical bleeding, naturally postmenopausal, as this is the common age of occurrence. In our patient, of twenty-one years of age, there had been a history of bleeding for one year, and then a short period of amenorrhea. In the case of Löffler and Priesel, at eighteen years, a similar history was obtained. In addition in our case the patient noted an enlargement of the breasts.

The uterus is usually enlarged and soft, and in those cases where the endometrium was obtained, it was hyperplastic. After the removal of the tumor all the symptoms regress.

While Löffler and Priesel report a case as malignant, all the other patients thus far reported have apparently been cured by operation. In all probability a unilateral oophorectomy is all that is indicated.

Here again is a distinct tumor type, histologically, chemically, and biologically, suggesting the undeveloped theca cell as its source of origin.

#### ARRHENOBLASTOMA

Virilism or masculinization in a previously normal female is a characteristic of a definite tumor type that is found in the ovary. At times somewhat similar pictures can be produced by tumors of the adrenal. Hirsutism alone has been described associated with granulosa cell tumors and even in women with no demonstrable lesion (Spielman).

Robert Meyer has attempted to group two types of ovarian growth under the common term arrhenoblastoma. He includes the so-called adenoma testiculare ovarii, first described by Pick, which he terms the typical form, and an atypical form, the true arrhenoblastoma, believing that both neoplasms have a common histogenesis.

The question raised by Pick is one of origin. He was of the opinion that the tubular adenoma, first described by him, arose in the testicular portion of an ovotestis. R. Meyer, however, believes that these adenomas, as well as the more atypical growths, arise from the embryonal vestigial remnants of the medullary cords

\*This study was carried on in collaboration with Dr. Rosenthal of the clinical laboratory, Mount Sinai Hospital.

and rete tubules of the ovary. He points out the fact that in the adenoma tubulare there are no evidences of hermaphroditism as one might be led to expect in an individual harboring an ovotestis.

The typical adenomas only rarely cause masculinization, while the atypical usually do. Meyer believes that this variation in physiologic effect need not imply a different origin, but merely a difference in the degree of development of the anlage. The masculinizing form of the tumor arises from cells that still retain the male hormonal influence which may be activated by some stimulus.

In fact, though the typical adenoma described by Pick and the atypical one of Meyer seem not at all related in morphologic appearance, in an intermediate group of six cases, five of Meyer's and one of Popoff's, Meyer showed various stages of transition from the tubular adenoma to the atypical form. In all the cases masculinization of the host appeared in varying degrees. This manifests itself in amenorrhea, masculine voice type, at times masculine carriage, and facial appearance, or hirsutism confined to the arms and legs and face.



Fig. 12.

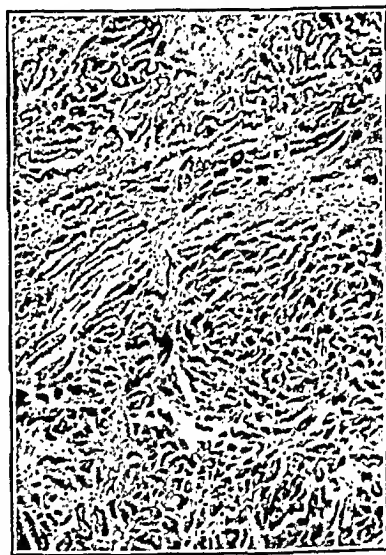


Fig. 13.

Fig. 12.—Intermediate type, regular and irregular tubules.

Fig. 13.—Intermediate type, solid cords and irregular tubules. (Same case as Fig. 12.)

The typical adenoma testiculare ovarii is usually a small tumor, firm, encapsulated, or embedded in the ovarian structure, and composed of regular tubules with a small circular lumen, lined by a layer of cuboidal cells, supported in a dense connective tissue. In one case reported by H. O. Neumann, the presence of cells resembling the interstitial cells of the testicle made the resemblance to the true testicular adenoma of the male gonad very striking.

The intermediate group of atypical tumors are larger growths than the typical ones, reaching the size of an adult head, and are unilateral. They have a lobulated surface, are encapsulated, smooth, and may infiltrate the surrounding structures. On section they are soft, medullary-like yellowish growths with a marked tendency to undergo regressive changes. Hemorrhage, necrosis, and liquefaction are present, and in some instances true cysts with an epithelial lining may be present. Some of these tumors may simulate cysts, and their true identity may be extremely difficult to establish. The tubules are irregular, their lumina varying in size and contour (Figs. 12 and 13). Some of the epithelial cells undergo fatty degeneration.

As the more atypical group is approached the tumor pattern (Fig. 14) varies markedly from the pure tubular or partly tubular and partly cellular-like growth of the intermediate type. In the main the tumor is solid with a few atypical tortuous tubular areas, or areas of convoluted solid cords of cells (Fig. 15). These cell cords can at times be recognized as composed of cells resembling the more sarcomatous appearing elements that may form the bulk of the growth. The stroma may become sarcomatous (Strassman). There are evidences of cyst formation with epithelial lining and even papillae (Robert Meyer), and Beuttner and Meyer have described mucinous epithelium.

As to the histogenesis, the probability of both tumor types, the typical and atypical, arising from the embryonal remains of testicular structures in the rete ovarii is most likely. However, the possibility of their origin, especially of the true adenomas, from a congenital ovotestis cannot be disproved.

The typical testicular type has no incertory function. Only in those tumors whose cells deviate from the normal do we have the presumed production of a masculinizing hormone.



Fig. 14.

Fig. 14.—Hemorrhagic tumor (Spielman's case).

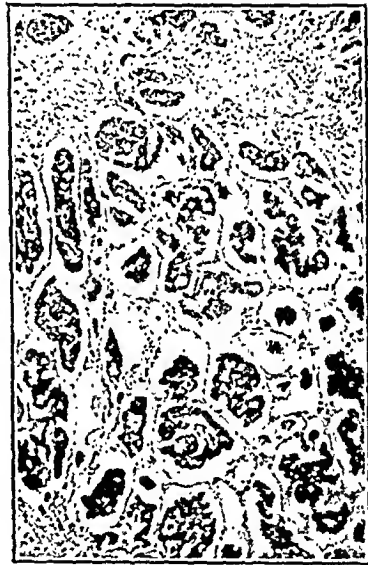


Fig. 15.

Fig. 15.—Atypical type with solid cords and tubules (Spielman's case).

Clinically these tumors affect the individual by, as before mentioned, changing her from a typical female to a masculine type. The menses cease, the breasts atrophy. The pelvic organs both external and internal likewise atrophy, except the clitoris, which may enlarge. There is a marked change in the facial appearance; it takes on a masculine appearance. Excessive hair development takes place on the face, especially on the upper lip, the chin, and the cheeks. Hair also appears on the chest and the extremities. The voice changes from the high-pitched feminine note to the deep low-toned male type, or may be cracked as in puberty. The gait is more that of the male stride than the mincing step of the female. The libido is adversely affected, and the normal interest in the opposite sex may disappear.

These symptoms with the removal of the tumor may subside. Cases are reported where pregnancy has supervened after the removal of the tumor, terminated by a



normal labor and a normal child (Sedlacek, Mathias, Neumann and Popoff). With the appearance of a recurrence the typical masculinizing syndrome may again be present.

While these tumors may present the histologic signs of malignancy, many of the patients have been successfully operated upon and permanently cured. Strassman reported thirteen cases, and all but one were malignant.

This tumor group is of distinctive histologic appearance and suggests the probability that the cells of the rete ovarii are the source of the neoplasm. In addition they present a typical clinical syndrome and probably contain a hormone that stimulates the development of the male characteristics, or negates the female influence, to permit some basic male principle to dominate.

#### DYSGERMINOMA

An unusual ovarian neoplasm is one previously called seminoma, by Chenat and Bender, because of its resemblance to the typical seminoma found in cryptorchids. Pick called it epithelioma-chorioectodermale. This type of growth occurs usually in a gonad that is functionally inefficient and has been described not only in the ovary and testis but also in ovotestis (Unger, Pick, and Polano). In addition, the host is not infrequently hermaphroditic as has been pointed out both by R. Meyer and H. O. Neumann.

The tumors may involve only one gonad or both. When one gonad is involved the other may be absent or so atypical that the identification of its type may be impossible. When both gonads are involved, they may be so completely replaced by tumor that it is impossible to determine the sex of the gonad. It must also be stated that in some instances the tumor may be present in a perfectly normal individual with a normal gonad on the other side, as in two of our cases.

E. Fauvet reports 27 cases from the literature in male or female hermaphrodites, 2 in true hermaphrodites, and 35 in normal women.

H. Kleine reported 7 cases, all in asthenic young women fifteen to twenty years of age. In one case the patient subsequently had one child, in another case two children.

We have had 3 cases, 2 in children twelve and fourteen years old, and one fifteen years old. The latter patient had menstruated normally for two years before operation. In the small fragment of ovarian tissue attached to a small mass of tumor from the second ovary, normal follicles, stroma, and corpora albicantia were present.

The tumors may reach the size of an adult head (Fig. 16). The surface has a capsule which may be intact or perforated by the growth, which then extends into adjacent structures. The surface may be smooth or bossed. Its consistency is elastic, though in places due to the breaking down of the growth and the formation of cysts it may be almost fluctuant.

On section it has a grayish yellow appearance, cellular, medullary, almost brain-like. Areas of necrosis, hemorrhagic and cyst formation may be found. Extension into the uterus and other gonad may be present, as in two of our cases.

Histologically the picture aside from the degenerative areas is strikingly uniform. The mass is composed of large round cells with a light granular cytoplasm and a round central nucleus. The cells are loosely arranged in columns and larger and smaller islands, separated by connective tissue strands. The connective tissue varies in amount, being scant in some places and better developed in others. In these strands, blood vessels are present, and numerous collections of small lymphocytes (Figs. 17 and 18). This latter characteristic is most striking.

The growth is most commonly found in children and young adults, usually individuals whose gonads are not functioning normally, so that as before mentioned,

hermaphroditic persons are frequently encountered. In addition, if the host is a typical female, the genitalia, both internal and external, may be infantile in type. It may occur in older women (Neumann), and Gross had a patient who had borne a child. It is usually unilateral, becoming bilateral only late in the disease.

The tumor apparently has no ineretory function and thus does not affect the individual either in a female direction as do the granulosa or theca cell tumors, or



Fig. 16.—Gross lobulated tumor.

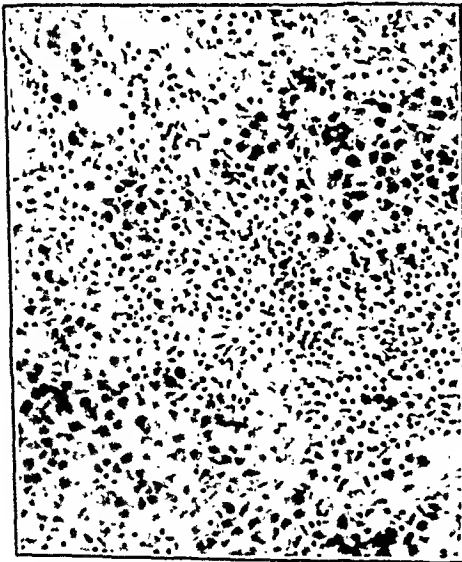


Fig. 17.

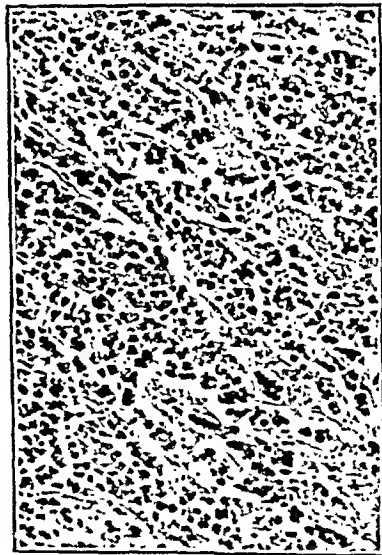


Fig. 18.

Fig. 17.—Cell cords and columns with scant loose connective tissue and lymphocytic infiltration.

Fig. 18.—Cell cords of large round cells with lymphocytic involvement.

in a masculine direction as does the arrhenoblastoma. These tumors apparently arise from cells probably of germinal epithelial origin which have lost their potentiality to become differentiated into either male or female cell types. In other words the cell of origin is a neutral cell, which can be classed as dysgerminal. It is from this term that R. Meyer suggested the name dysgerminoma.

Clinically the tumor causes no definite symptoms other than those of any pelvic growth. It is again to be stressed that the physical make-up of the host, either a pseudohermaphrodite or a young patient with atrophic genitalia, suggests the diagnosis.

The tumors are malignant, and unilateral removal may result in early recurrence or metastases in the retroperitoneal lymph nodes, the other ovary, peritoneum, pleura, or omentum. We have had occasion to operate upon several of these patients, and have found that operation followed by radiotherapy offers an excellent chance of permanent cure.

Robert Meyer has had patients who have survived four, six, and eight years, respectively.

To recapitulate, we have described four groups of tumors.

1. The granulosa cell tumor arising from unused granulosa cell forerunners in the ovary. These tumors have a definite intercretory function: they store or produce the estrogenic hormone. They affect the host by exaggerating certain aspects of the female physiology. They cause an increase in amount and frequency of the uterine bleeding. They stimulate the growth of the breasts and uterus, and cause a hyperplasia of the endometrium, in other words an overfeminization of the individual.

2. The theca cell tumor represents a group arising from the forerunners of the theca interna cells. These tumors in their biologic aspect are similar to the granulosa cell tumor, but are commonly found in the postmenopausal period, and differ so in other aspects from the granulosa cell tumors as to warrant their being regarded as distinct from this group.

3. The arrhenoblastoma is a neoplasm which arises from male-directed elements which have remained quiescent in the ovary, or as Piek believes from the male portion of an ovotestis. These growths presumably contain a male sex hormone, though this as yet has not been proved. They affect the host by causing a defeminization or as some express it a masculinization with the development of male hair type, male gait, voice, and larynx. The loss of the female breast contour, the loss of menstruation, and the atrophy of the genitalia also occur.

4. The dysgerminoma arises from neuter cells of germinal epithelial origin, i.e., dysgerminal elements. It has no intercretory function and no pathologic physiologic effect on the host, but is found often in individuals with defective gonads and atypical somatic development.

Investigation of tumors of the ovary with these points in mind may help us to understand better the physiology of the normal gonads and enable us to classify ovarian neoplasms more definitely.\*

100 EAST SEVENTY-FOURTH STREET

---

\*Note: For lack of space the extensive bibliography cannot be included but may be found in the author's reprints.

## THE TOXEMIAS OF LATE PREGNANCY\*

WILLIAM A. THOMAS, M.D., EDWARD D. ALLEN, M.D.,  
CARL P. BAUER, M.D., AND M. R. FREELAND, PH.D., CHICAGO, ILL.  
(From Rush Medical College and Presbyterian Hospital)

THE studies here reported arose from the application of the principles and knowledge utilized in our nephritic studies to the problems encountered in the toxemias of late pregnancy.

All patients, private and in the prenatal clinics, exhibiting any deviation from normal, such as hypertension, albuminuria, headache, visual disturbances, or edema, were hospitalized and subjected to intensive study, and the studies repeated as frequently as the condition warranted.

We have selected those tests which most accurately represent the various changes found in the toxemias and applied these tests to ascertain more definitely,

1. In which cases pregnancy must be terminated.
2. Which cases may be safely carried on with the object of obtaining a viable child.
3. In what form the toxemia will manifest itself should pregnancy continue.
4. The degree of permanent damage suffered by the mother in the cases allowed to progress.
5. The effect of toxemias on infant mortality.
6. To distinguish between toxemia, and nephritis occurring as an entity during the course of pregnancy.
7. In particular to evaluate the efficacy of the procedures used in preventing and combating this condition.

It becomes increasingly clear that the toxemia of pregnancy is not a definite entity, following a fixed course and governed by predicable rules. For example, it has been extensively taught that toxemia occurs most frequently in the first pregnancy and that one attack usually confers immunity. Our experience shows this to be far from the case. Many of the severe cases occur after several normal pregnancies; in others, successive pregnancies exhibited earlier and more severe manifestations.

The course of the disease may vary to any extent in severity and clinical manifestation, depending upon the tissues bearing the brunt of the damage. These causes may be toxic infections or metabolic. There is no single test which accurately represents this damage, since

\*Read at a meeting of the Chicago Gynecological Society, May 17, 1935.

This work was carried on with a grant from the Anna Louise Raymond Fund.

one will give entirely normal results while others show evidence of extreme disability. In both these conditions, understanding comes from painstaking analysis of all findings, clinical and laboratory, and a correct correlation of the tests and their significance.

Our studies indicate that in these toxemias, certain tissues or tissue aggregates are particularly susceptible to injury; that the degree of involvement of each is distinctly independent of all others; and that certain tests are definitely valuable in ascertaining the functional state of each of these systems. To be more concrete, toxemias manifest themselves in a great proportion of cases by involving one or more of the following tissue aggregates, each with its own peculiar train of symptoms dominating.

I. *Vascular-renal*: resembles nephritis; blood in urine, albumin, hypertension, retinal changes, spasm and exudate if severe.

II. *Central nervous system*: eclamptic; headache, nausea and vomiting, convulsions.

This type possibly involves posterior pituitary with increase of pressor and anti-diuretic principles. This may occur with or without hypertension, possibly dependent upon posterior pituitary involvement. Hypertension of this type is distinctly different from pure vascular or nephritic type and response to treatment differs.

III. *Tissue type*: resembles nephrosis; general involvement of nonspecialized tissues, edema and albuminuria, frequently without hypertension of headache.

IV. *Liver*: prostration; nausea and vomiting; convulsions, shock (collapse and death), with hypotension; either antepartum or postpartum.

Obviously, these four systems may be involved to approximately equal degree or there may be any degree of individual variation. Consequently, a test which accurately represents the grade of incapacity of one group is in no sense an index of damage elsewhere. It becomes necessary to take definite issue with those who advocate any set test or tests as representing the true state of these patients. One group of investigators adheres absolutely to the urea clearance test, setting arbitrary limits below which all patients are in a hazardous condition and above which there is little cause for concern. From another source comes a fixed system of blood pressure readings, and cases are rated according to the strata into which their systolic pressures delegate them. Any such complacent attitude gives either a false sense of security or an unjustifiably grave outlook, for reasons already stated. Unless one is familiar with and competent to judge the interpretation and significance of any or all of these methods of precision, he will do better to proceed on the clinical basis, with due regard to all the manifestations. The errors liable to be encountered in this latter method will be referred to later (circulatory asthenia, etc.).

For example, there very recently came into the hospital a multipara at full term with a history of 6 normal pregnancies. On admission her pressure was 260/140:

albumin +++; she was almost totally blind and retinal examination revealed extensive exudates with high degree of retinal vessel involvement. The routine tests were hurriedly made and labor induced. Two urea clearance tests of 140 per cent and 110 per cent (average 125 per cent) and liver function of normal indicate the fallacy of relying upon the former in such conditions. Repeatedly, patients with urea clearances far below accepted limits of normal have been successfully carried to term, while others with entirely satisfactory urea clearance tests have progressed to such a grave state by clinical and other standards that there remained no choice but to terminate the pregnancy.

Another group of cases has been of great interest. These women, seen in the clinic, with large amounts of albumin in the urine, enter the hospital at once. On the following morning the urine is consistently free of albumin while in bed. Urea clearance figures are high, often 200 per cent or more, and all other tests are normal. These women are definitely a type of circulatory insufficiency. Their hearts are always normal, never decompensated, but often small for their size (for they are usually obese), but the outstanding feature is probably the fact that their arteries and systemic circulatory apparatus are inadequate for their bulk, particularly under the increased load of pregnancy and normal activity. Undoubtedly many such cases are considered as impending toxemias and aborted. Such cases have been repeatedly hospitalized for tests and, following delivery, apparently have normal findings. Thus, albuminuria, even in extreme quantities, may not be of specific significance in pregnancy.

At this point it seems reasonable to emphasize certain facts that are evident to students of nephritis and to call attention to a more abstract but significant theory. This theory removes from the realm of renal insufficiency definite clinical phenomena and places them in the extrarenal or tissue field. In the first place, it is generally evident that neither the external phase of water balance, represented by excretion, anuria, diuresis, and their variations, nor the internal phase, chiefly edema and dehydration, are to any great degree dependent upon ability of the kidneys to excrete water, but parallel much more closely the state of protoplasm, represented by cellular activity, electrolyte distribution, metabolic disturbances, and activities of various glands of internal secretion.

Second, it is becoming increasingly evident that the concentration of electrolytes and metabolites in the blood, that is, blood chemistry readings, is in no respect a function of renal capacity, but represents the level at which osmotic equilibrium occurs between tissues and blood. This means that we have no direct concern with the levels of blood chemistry, except so far as they accurately represent the tissue and cellular concentrations, and that whatever clinical symptoms occur synchronously with elevated blood chemistry findings are due to the tissue concentration of these metabolites, rather than to their

accumulation in the blood. To make the analogy complete, failure of the kidneys to excrete water is not due to renal inability, but to primary claim of tissue thirst on the free blood water. Diuresis will occur, without renal change, whenever the state of tissue metabolism so improves that tissue-bound water is released and this water returning to the circulation is again available for renal excretion.

Similarly, when, due to disturbances of cellular metabolism, such changes occur so as to result in tissue accumulation of electrolytes and metabolites, there must result an osmotic equilibrium between blood and tissues before there are excess substances for renal excretion. As long as the tissue pathology results in this excess content, so long will the blood figures remain elevated. Should any improvement in this tissue state decrease their abnormal content, releasing into the blood the accumulated metabolites, the kidneys will in practically all states excrete this excess, so that the blood figures will reflect the improved tissue state.

Let us visualize two men: one entirely normal with urea nitrogen of 10 mg. and nonprotein nitrogen of 25 mg. per 100 c.c.; the other a chronic but stabilized case of Bright's disease, with urea nitrogen of 40 mg. and nonprotein nitrogen of 100 mg. per 100 c.c. For one year, each is given an identical diet with 100 gm. of protein daily, following which blood chemistry findings are identical with those of a year before. Have the kidneys of one or the other done more work in excreting end products of protein metabolism? The answer is obviously that each has done the same. Furthermore, had the nephritic patient had a markedly lower protein allowance, his final blood chemistry levels would not have been modified, and clinical experience indicates that had the level of protein feeding been increased there would have been no additional accumulation in the blood.

Two conclusions may be drawn from these facts: (1) that the level of blood chemistry determinations is not a function of renal activity, but of the state of tissue integrity; and (2) that the high urea clearance figures in the women with circulatory insufficiency are due, not to any extraordinary capacity of kidneys, but to the release into the circulation, available for excretion, of urea that had accumulated in the tissues during a period in which these tissues were in a sub-active state.

These facts naturally throw some doubt upon the validity of the conception of the urea clearance test as a definite function of glomerular activity or capacity and suggest that it may indicate more definitely the state of tissue activity. In any event, this and other accumulating evidence is sufficient to justify its rejection as the *sine qua non* of toxemias.

Furthermore, the problem of blood sugar raises significant points. Episodes of two types may occur: transient glycosuria associated with elevation of blood sugar, especially in the earlier months of pregnancy; and persistent hypoglycemia in the later stages, particularly in the toxemias. Fundamentally, these fluctuations have been attributed to pancreatic disturbances. Recent investigations (see Collip, J. A. M. A., March 9, 1935) indicate a close relationship between activity of the anterior pituitary and the pancreas. Since abnormal activity of the anterior pituitary is increasingly evident in toxemias of pregnancy, some correlation between that function and the blood sugar may be discovered. Furthermore, the liver as the principal organ in removing glucose from the blood, synthesizing it as glycogen and releasing it upon appropriate stimuli, being frequently the seat of extensive damage in these conditions, may itself be responsible for the lowered blood sugar so constantly found. These surmises are not only theoretical, but may point the way to a clearer understanding of the basic derangements causing toxemias of pregnancy.

With these considerations as a background, a brief summary of our conclusions is given:

*Blood chemistry levels*, with the exception of blood sugars, have been of no importance in these states, except to designate as nephritic those cases which clearly fall into that class either as preexisting Bright's disease or as the latent condition aggravated by the metabolic load of pregnancy. Even the type of toxemia previously designated as nephritic does not show any degree of accumulation of metabolites. (This is in accord with the conclusions of numerous investigators.)

*Urea clearance test*, when considered as a relative index, possibly of renal damage and probably of tissue disturbance, is a valuable guide. There is no critical level, and its value lies in repeated tests to determine its trend. The condition may be most grave in the presence of high urea clearance, and favorable even when reduced to quite low levels. The progressive decrease of clearance is regarded as ominous.

*Liver function*: Numerous satisfactory liver function tests are reported from various sources, with few exceptions, however, related to toxemias of this type.

Bilirubin clearance and bromsulphalein are highly regarded in some quarters.

In our hands the galactose tolerance test is of no value whatsoever, since it is very insensitive and extreme liver damage (both clinical and by other tests) occurs before the galactose test gives any indication of damage.

After numerous trials, we found the Rose-Bengal test most accurately to represent the functions in which we are interested. It is simple, inexpensive, easily read either by spectroscope or colorimeter, and gives early and accurate evidence of the liver type of damage



which leads to one of the severe and serious types of toxemic manifestations, namely, convulsions, shock, and collapse.

*Skin absorption time*, as advocated by McClure and Aldrich, is of the same significance as in Bright's disease, an evidence of edema, either impending or decreasing, and represents accurately changes in tissue thirst. In extensive edema, it indicates whether or not therapeutic measures are succeeding, and absorption time shorter than normal, in the absence of definite edema, warns of tissue damage and probability of ensuing edema.

*Concentration tests and modified Mosenthal* are of the same significance as in nephritis. They do not indicate integrity or impairment of renal function, but hydrophilic state of tissues.

*Serum proteins*: decrease of total serum protein, or reversal of albumin/globulin ratio, while not the sole cause of edema, facilitates its appearance, with symptoms dependent on the tissues involved, central nervous system, anuria, ascites, or general. This appears more commonly with inadequate protein in the diet.

These tests and principles are applied to suspected or potential toxemias and, so far as possible, to these same patients at the end of the puerperium, just preceding discharge from the hospital, and at intervals for years, either in subsequent pregnancies or by hospitalization for a brief period at intervals of three, six, and twelve months, or whenever they can be prevailed upon to submit to the tests. In addition, we are hospitalizing and testing cases with definite toxemias occurring prior to the initiation of this work, and searching for evidence of actual or latent damage.

Outstanding in all this work is the fact that no test or group of tests accurately represents the complete picture of toxemia of pregnancy, and that clinical experience and judgment must not be relegated to a position secondary to any arbitrary set of standards. We are learning to more accurately judge the value of the tests; to discriminate in cases where all findings are not in accord; learning how far cases may be carried without immediate jeopardy to mother or child; what the remote consequences of the prolongation of the toxemic states are; learning the efficacy of the various therapeutic procedures; and discarding from the category of toxemias cases that have previously been so considered.

#### THERAPY

After complete tests are finished, patients are put on a salt-free diet. During pregnancy there is an invisible edema which is aggravated by the sodium ion, and diuresis and loss of weight occasionally follow this procedure alone. Potassium chloride, 2 to 3 gm. daily, is given on the tray, to be used as salt, and this definitely decreases edema in many instances.

TABLE I\*

PATIENT	DATES	ALBUMIN		BLOOD PRESSURE		ROSE-BENGAL		UREA CLEARANCE PER CENT		EDEMA		PSP	
H.	5/34-4/35	++ +	0	130/100	120/ 80	77-50	60-40	44	82	0	0	--	--
R.	5/34-3/35	++ +	0	160/100	125/ 80	45-20	50-35	38	74	0	0	--	0
R.	3/35-5/35	0	0	155/100	112/ 74	53-30	--	16	135	++ +	0	63	--
D. P.	8/33-3/35	++ +	0	200/120	110/ 75	--	--	--	58	++ +	0	--	--
H. R.	7/33-3/35	++ +	tr.	110/ 70	120/ 70	--	--	85	85	++ +	0	58	--
S.	11/33-3/35	++ +	+	180/130	140/100	--	--	85	25	0	0	60	50
S. P.	12/33-4/35	++ +	0	170/110	120/ 80	--	--	70	--	++ +	0	67	--
G.	12/33-4/35	0	0	140/ 90	110/ 80	--	--	--	--	0	0	--	--
Bl.	12/33-4/35	++ +	0	170/110	148/ 90	--	--	100	--	++ +	0	75	--
H. O.	9/33-4/35	++ +	0	110/ 70	110/ 70	--	--	80	--	0	0	100	--
F.	9/23-3/35	++ +	0	164/110	115/ 80	--	67-35	--	50	0	0	--	60
O.	1/29-4/35	++ +	0	200/130	140/ 90	--	43-28	--	50	++ +	0	--	63

\*Results of retesting after delivery: First column under each heading is before delivery; second column subsequent to delivery. Cases in which tests were satisfactory were not repeated in some instances.

Case S was allowed to continue pregnancy for four months because of desire for child and now has definite vascular and renal damage. The last two cases had eclampsia. In first pregnancies, and again in subsequent pregnancies. At present they show evidence of some damage. All others apparently are normal.

*Adequate Protein Diet.*—Usually 100 gm. is given daily in women of average weight. If there is excessive loss as urinary protein, additional protein is given. If serum proteins are low, larger protein feedings may raise the level or at least aid in preventing further lowering of this level. Protein is given as meat, milk, eggs, and cheese. There is no evidence that meat in the amounts allowed is harmful.

*Fluids* are given freely, even in the presence of edema. Since edema is due to tissue thirst, which must be satisfied before there is available much water for renal excretion, toxins can best be washed out by liberal administration of fluid.

*Sedatives.*—Potassium bromide and barbiturates are used in the pre-eclamptic stage, particularly the hypertensive type.

*Magnesium Sulphate.*—Ten per cent solution intravenously is very effective in reducing excessive blood pressure. The result may be brief, in which case the medication may be repeated.

*Glucose* in 6 per cent or 10 per cent solution intravenously or by multiple needles subcutaneously, is of value in hypoglycemia and anuria, and hypertonic glucose is valuable in edema of the brain accompanying convulsions in eclampsia. By supplying tissues with adequate nourishment, supplemented by small doses of insulin, marked improvement in metabolism may result, releasing water from tissues. A liberal carbohydrate diet is given by mouth, with no attempt to control fetal weight.

*Calcium* as lactate by mouth, and gluconate or levulinate intravenously protects against liver damage, and by replacing sodium from tissues, promotes diuresis.

*Venesection* is avoided at all costs. Tissues are suffering from a sub-oxidative state, and removal of oxygen and food-carrying tissue is harmful to the organism. Other methods for attack of special symptoms should be utilized.

*Shock*, one of the toxemic manifestations occurring usually just postpartum, occasionally antepartum, is due to rapid loss of blood volume, not as hemorrhage, but depletion of free blood water by tissues. The primary need is a fluid that will remain in the circulation. Salt and glucose solutions are lost almost as rapidly as given. Blood transfusion or acacia solution are the two forms of fluid which conform to these requirements, and improvement during the course of acacia administration is frequently very striking.

To combat the hypotension, adrenalin repeatedly, strychnine in doses of 1/10 grain, and caffeine are all valuable and may be used at the same time. Oxygen is of great assistance in the cyanosis and dyspnea of shock.

The above 62 cases (Tables II and III) constitute the cases of toxemias which manifested symptoms sufficiently severe to warrant hospitalization.

Column A in Table III represents 35 patients in whom toxic manifestations appeared early in pregnancy. These cases were carried along on treatment and had repeated functional tests. When symp-

TABLE II  
MATERNAL DEATHS

	NUMBER OF CASES		TOTAL	EXPRESSED IN PER CENT		
	35 A	27 B	62 C	35.0 A	27.0 B	62.0 C
Primipara	12	14	26	34.2	51.8	41.9
Multipara	23	13	36	65.8	48.2	58.1
Spontaneous onset of labor	27	16	43	77.1	59.2	67.7
Induction, castor oil, quinine	5	4	9	14.2	14.8	14.5
Induction by bag	1	1	2	2.8	3.6	3.3
Normal deliveries	24	18	42	68.5	66.6	67.7
Forceps	1	4	5	2.8	14.8	8.0
Breech	2	2	4	5.6	7.2	6.4
Twins	1	0	1	2.8	0	1.6
Version and extraction	1	0	1	2.8	0	1.6
Vaginal hysterotomy, craniotomy	1	0	1	2.8	0	1.6
Cesarean section						
Low cervical	6	2	8	16.8	7.2	12.9
Porro sections	1	0	1	2.8	0	1.6
Indications for section				5.6	7.2	12.9
Pelvic	2	2	4	33.2	66.6	50.0
				2.8	0	1.6
Previous section	1	0	1	16.6	0	12.5
				8.6	0	4.6
Toxemia	3	0	3	49.8	0	37.5

TABLE III  
FETAL DEATHS

	NUMBER OF CASES		TOTAL	EXPRESSED IN PER CENT		
	35 A	27 B	62 C	35.0 A	27.0 B	62.0 C
Premature births	13	5	18	27.1	14.7	29.1
Term births	22	22	44	62.9	85.3	70.9
Average weight of babies	6 lb. 4 oz.	6 lb. 1 oz.	6.0 lb. 2.5 oz.			
Gross infant mortality	10	3	13	28.5	11.1	20.9
Term baby deaths	2	0	2	20.0	0	15.3
Premature deaths	8	3	11	80.0	100.0	84.7
Antenatal deaths	3	2	5	30.0	67.0	39.5
Postnatal deaths	7	1	8	70.0	33.0	61.5
Maternal deaths	0	0	0	0	0	0
Sepsis	1	2	3	2.8	7.2	4.9
Eclampsia	2	1	3	5.6	3.6	4.9
Intrapartum	0	1	1	0	3.6	1.6
Postpartum	2	0	2	5.6	0	3.2
Antepartum	0	0	0	0	0	0

toms and tests gave evidence of severe disturbance, pregnancy was terminated artificially in this group. The other patients in this group went into labor spontaneously at term or prematurely. Many of these

cases were carried for months. This group necessarily is composed of the serious types of toxemia.

Column B is composed of 27 patients who, for the most part, exhibited toxic symptoms late in pregnancy. These cases, except for two, were mild toxemias.

The only reason for continuing pregnancy in the face of a toxemia is in interests of the child. It was hoped that by careful clinical observation and frequent functional tests, patients exhibiting a toxic state early in pregnancy could be carried with fair degree of safety to approximately term. This was accomplished in about 60 per cent of the cases. The other patients either delivered prematurely or the pregnancy had to be terminated prematurely.

At the present time, all that can be said for 35 patients in Group A is that about 60 per cent will carry to viability, 40 per cent will deliver prematurely or will necessitate termination of pregnancy before term, 33 per cent will lose their babies, and 20 per cent will probably suffer some latent damage.

#### CONCLUSIONS

1. Toxemia of pregnancy is a generalized, systemic manifestation of an as yet unknown agent, these manifestations appearing in one or more systems, each with its individual symptoms, with tests more or less specific for each of the systems.

2. There is no test which alone is of value in determining the severity of the condition and each test must be interpreted in the knowledge of the field to which it applies.

3. In the aggregate, the tests enumerated give valuable information regarding the status, progression, value of therapy and degree of recovery. Taken collectively in conjunction with clinical observations, they may safely be the basis of accurate decisions.

---

Gery, L., and Adrian, J.: Statistical Study of Tumors of the Ovary. Report of Five Hundred Cases, *Bull. Soc. d'Obst. et de Gynéc.* 24: 310, 1935.

The authors studied 506 ovarian tumors. In listing them they follow the classification of P. Masson. They found that 42.6 per cent were tumors of the ovarian tissue proper, chiefly cysts; 27 per cent were wolffian tumors; 8.2 per cent mesenchymal newgrowths; 14 per cent cystic teratomas; 2.4 per cent metastases, and in 5.8 per cent the type of tumor could not definitely be determined.

The authors conclude that it is difficult to make a prognosis from the histologic diagnosis. However, of the 506 cases, 51.4 per cent were histologically benign, 38.5 per cent were histologically malignant, and in 10.1 per cent differentiation not definite.

J. P. GREENHILL.

# TREATMENT OF VESICOVAGINAL FISTULAS\*

## PAST AND PRESENT

NORMAN F. MILLER, M.D., ANN ARBOR, MICH.

ALTHOUGH the incidence of vesicovaginal fistulas is not accurately known, there is evidence to warrant a possible belief that its decrease as a result of improved obstetrics is balanced by a higher incidence following pelvic surgery. The fact that, today, large series of cases are seldom reported does not refute this belief. Instead, it may be taken as an indication of the fact that surgeons everywhere are attempting repair of fistulas whereas in former years individuals so afflicted generally gravitated to larger centers where this type of work was being done successfully. Failure following attempt at repair is still common. To this many individuals will testify, and one need only inspect patients' records to realize that many unsuccessful operations may pave the path to ultimate relief. Because of these things and because of a firm belief in the fundamental truth voiced by Dr. George Gray Ward,<sup>152</sup> who seventeen years ago commented thus: "The most successful surgeon of the future will be he who, with a wide knowledge of all the methods at his command, chooses the one which will be most suited to the individual case." I desire to present a survey, a panorama as it were, of the treatment of vesicovaginal fistulas, leaving for another time a similar contribution on the even more interesting group wherein the urethra and bladder sphincter are involved.

While vesicovaginal fistulas have existed since the beginning of mankind, probably the earliest tangible evidence of its occurrence was the discovery by Professor Derry of a large vesicovaginal fistula in the mummy of Queen Henheit, one of the wives of Mentuhotep who reigned about 2050 B.C. (Bey<sup>14</sup>). Hippocrates (460-377 B.C.) mentioned the involuntary discharge of urine following some confinements but said nothing of its cause (Agnew<sup>5</sup>). Bey credits Avicenna (A.D. 1037) with the first accurate description of the lesion. In 1582 Ambrose Pare<sup>5</sup> discussed fistulas in general but did not mention vesicovaginal fistulas. Later in the sixteenth century Louis de Mercado, Felix Plater, and Severin Pineau all gave a clear description of the lesion.<sup>87</sup>

Earliest mention of treatment probably appeared in the Ebers Papyrus (Bey), where several prescriptions are given for the cure of incontinence of urine in women. Aside from spontaneous healing which was probably attributed to the influence of prevailing mystic concoctions of legendary interest, no real step toward the correction of this dreaded condition is recorded until the latter part of the seventeenth century when, in 1672, van Roonhuiyse of Amsterdam first presented a well-defined remedial plan.<sup>87</sup> His method is of more than usual

\*Presented, by invitation, at a meeting of the New York Obstetrical Society, February 12, 1935.

interest, since it was probably the first recorded operative procedure for vesicovaginal fistulas. Van Roonhuyse advised denudation of the edges of the fistula with scissors or knife and their approximation by use of pins made of strong sharpened goose quills which were properly wrapped with red-waxed silk and coated with a healing salve. Dressings of flat wicks moistened in warm balsam oil were then applied and the vagina filled with suitable sponges moistened in a little oil of sweet almonds (Kelly). Because of his clear description and familiarity with fistulas, Kelly believes van Roonhuyse actually operated upon patients by this technic. About seventy-five years elapsed before the next significant mention of treatment was made. In 1752 Johannes Fatio<sup>87</sup> spoke of pulverizing live toads in a new pot, the product to be placed in a bag and worn around the abdomen; but stated that he preferred surgical methods and mentioned curing several fistulas by the van Roonhuyse technic.

Progress during this earlier period was slow but the darkness was thinning and, at the beginning of the nineteenth century, there dawned a new day in the treatment of vesicovaginal fistulas, which reached its zenith half a century later in the great contributions of Jobert (de Lamballe<sup>76-79</sup>), Wutzer,<sup>158, 159</sup> Simon,<sup>137-139</sup> Sims,<sup>140, 141</sup> Brown,<sup>25, 26</sup> Emmet,<sup>50-52</sup> Bozeman<sup>20-24</sup> and others. Prob-

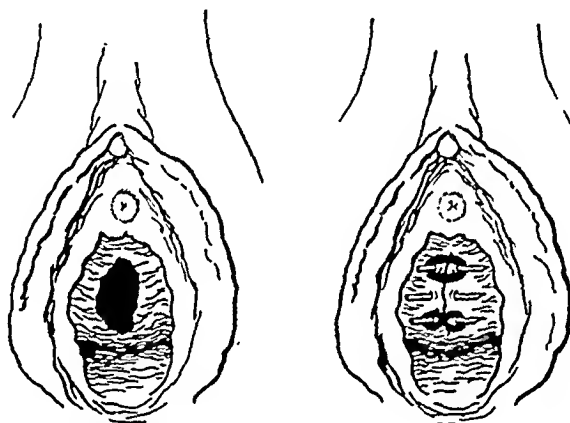


Fig. 1.—The use of sharpened goose quills as a means of approximating the edges represents the earliest type of operative procedure for the correction of vesicovaginal fistula. (Von Roonhuyse, 1672.)

ably the first record of importance in this new era is that of Desault,<sup>9</sup> who in 1804 obstructed the opening with a plug (sphere of gum elastic) or valve covered with wax, using at the same time a large catheter retained in the bladder by means of a truss. About this time Dupuytren first recommended caustics and cautery. Vidal (de Cassis<sup>9</sup>) invented a spring forceps for approximating edges of the fistula, while Naegele<sup>9</sup> (1812) made an extensive study of the condition and attempted repair. Later (1822) he pared the edges and approximated with interrupted sutures. In James's *System of Midwifery*, published in 1813, we find the use of an elastic catheter advised to aid spontaneous healing. James also mentioned using a cautery where the opening was small, and spoke of freshening the edges and employing a catheter where the opening was large. Vidal (de Cassis<sup>9</sup>) recommended closure of the vulva. In 1829 Levert,<sup>122</sup> of Mobile, experimented with metallic sutures and in the same year Malagodi<sup>9</sup> of Bologna pared the edges of fistulas and approximated with suture. Similarly, Diffenbach,<sup>9</sup> using a speculum for better exposure, pared the edges and approximated with lead or wire sutures. Gosset<sup>9, 65</sup> (1834) used gilt wire for closing fistulas. Professor Roux (1829) proposed the knee-elbow posture for better exposure, but postural exposure and the gutter speculum are thought to have been

known and used by Schreger as early as 1817. Soon afterward posture was adopted by Ryan<sup>130</sup> and by Wützer<sup>158, 159</sup> (1834).

Barter<sup>122</sup> (1836) placed patients in the knee-elbow position when cauterizing fistulas, and Liston mentions the use of this position in 1838. In Dantzig, Wagner<sup>9</sup> (1834) described splitting the posterior edge of the opening and placing in this cleft the beveled anterior edge. In the same year, Wützer of Bonn systematized the operative treatment and emphasized the importance of posture for exposure during operation as well as for drainage during the postoperative period. He not only pared the edges of the fistula and approximated with suture using knee-elbow posture for exposure but performed suprapubic paracentesis and kept the patient on her abdomen during the postoperative period for better drainage. In 1848 Wützer reported eighteen patients operated upon, with three cures.

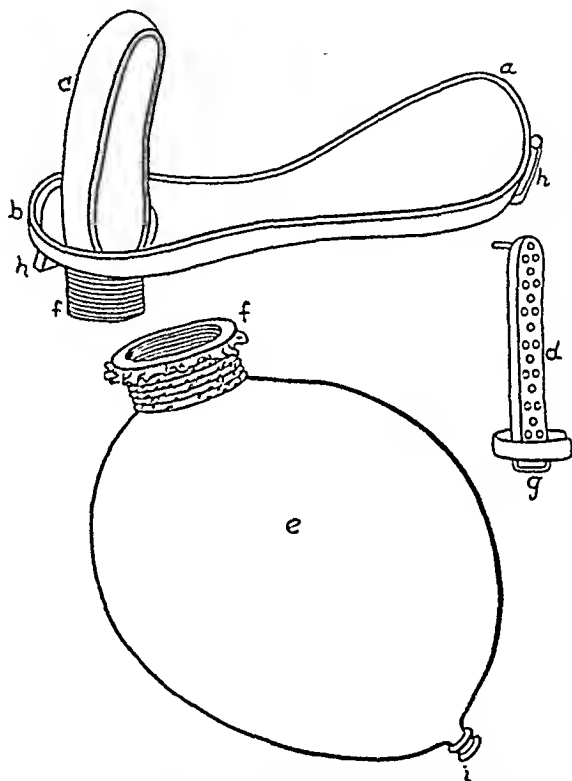


Fig. 2.—This early type of urinal was designed with an intravaginal extension to fit over the opening of the fistula.

In our own country the first record of operative closure is attributed to Hayworth,<sup>5</sup> who (1839) freshened the edges of the fistula and approximated with thread sutures. Later he reported a total of twenty patients treated with three cures (Agnew<sup>5</sup>).

In 1846 Metzler<sup>9</sup> of Prague combined many of the suggestions made up to that time. He placed his patients in the knee-elbow position, used a right-angled speculum, and approximated the denuded edges with gilded needles held in place by clamps of shot. Postoperative drainage was provided by a catheter in the bladder. In the same year, Pancoast in Philadelphia used a split flap method. Mettauer<sup>122</sup> in Virginia used lead wire for approximating the edges. Luke<sup>9</sup> of Charing Cross Hospital used silver wire for the same purpose in 1850.

Interest in the treatment of vesicovaginal fistula had now gained considerable momentum and much credit for this must go to Jobert (de Lamballe)<sup>76-79</sup> of Paris who about 1834 attempted to transplant tissue flaps from the vulva as a stop-gap.



In 1845 he cut the bladder free from the cervix in order to minimize tension and in 1849 reported thirteen cures. He was perhaps the first to emphasize the importance of avoiding tension. To this end he not only attempted mobilization of the bladder but made incisions in the vaginal mucous membrane. Maisonneuve, following the teaching of Jobert (de Lamballe), was able to cure a case where the whole anterior wall of the vagina had disappeared.

Nearing the peak of this new era, we now find Simon,<sup>137-139</sup> in Germany, following the precepts of Jobert but improving upon his technic by substituting tension sutures for vaginal incisions. Simon became a recognized leader in this type of work. In 1854 he was able to report cure in thirty-five of forty patients operated upon. Simon, interestingly enough, used an exaggerated lithotomy

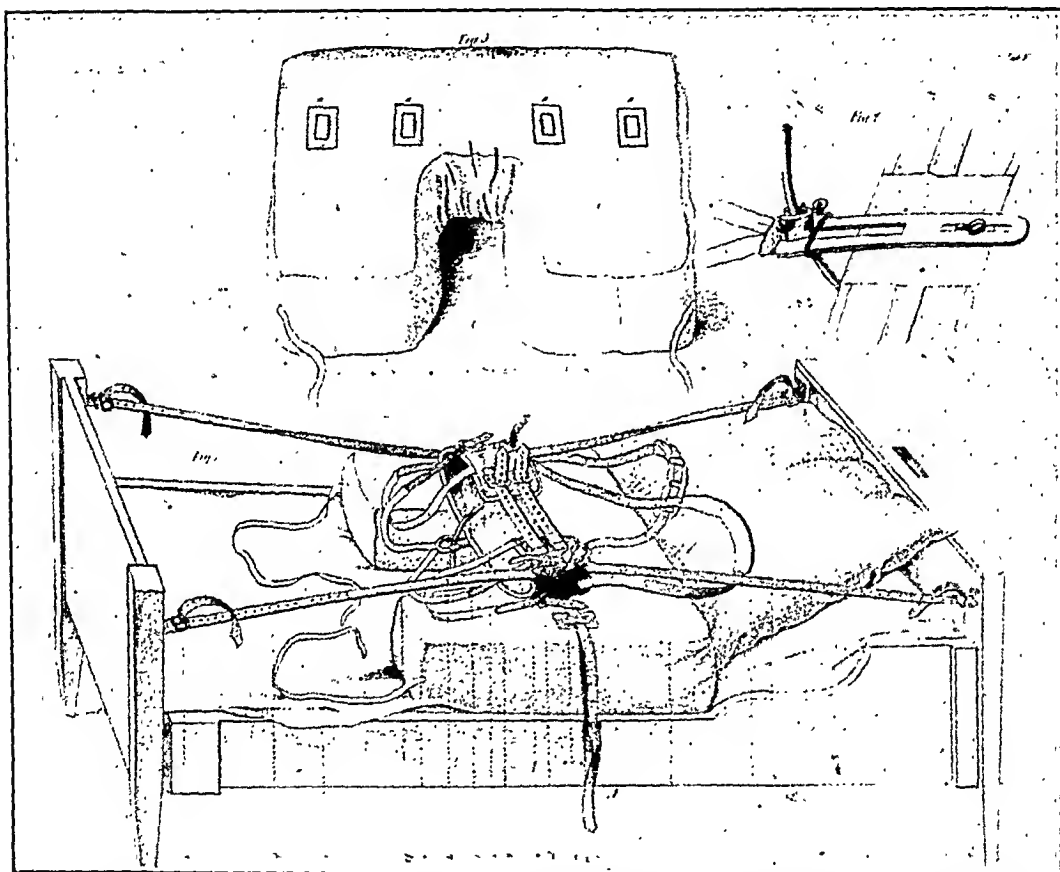


Fig. 3.—Bed and harness designed in 1842 by the unrecognized genius Wutzer, for the purpose of maintaining the patient in the knee-chest position during the long exhausting time required for operation.

position and paid little attention to postoperative care, using no drainage and often permitting his patients to be up a few days following operation. About this time America was destined to witness the début of one of its most famous surgeons. For in 1852 J. Marion Sims'<sup>141</sup> now famous article, "On the Treatment of Vesico-Vaginal Fistula," appeared in the *American Journal of the Medical Sciences*. Sims quickly became a recognized master in this work, his fame spreading the world over. He emphasized adequate exposure which he obtained by use of the "Sims' speculum" and "Sims' position." Denudation of the edges and approximation with silver wire were essential parts of his technic. Postoperatively he considered five things important: (a) The use of a block tin catheter for continuous drainage; (b) bowel to be kept quiescent for ten to

fifteen days; (c) opium; (d) normal fluids, (e) perineal irrigations. The success of this remarkable surgeon will be more fully grasped when we realize that eight years after his initial operation he was able to report on a series of 261 cases with cure in 81.9 per cent (Rawls<sup>125</sup>). The fascinating story of his trials and worries is to be found in his publications and in the story of his life. The fact that after forty operations on his first three patients he failed to achieve a cure, shows that his rise to fame was not without struggle and tenacity of purpose on his part. In Thomas Addis Emmet,<sup>50-52</sup> Sims' successor at Woman's Hospital, New York, the world was quick to recognize a master of the highest caliber. So skillful did Emmet become in the treatment of vesicovaginal fistulas

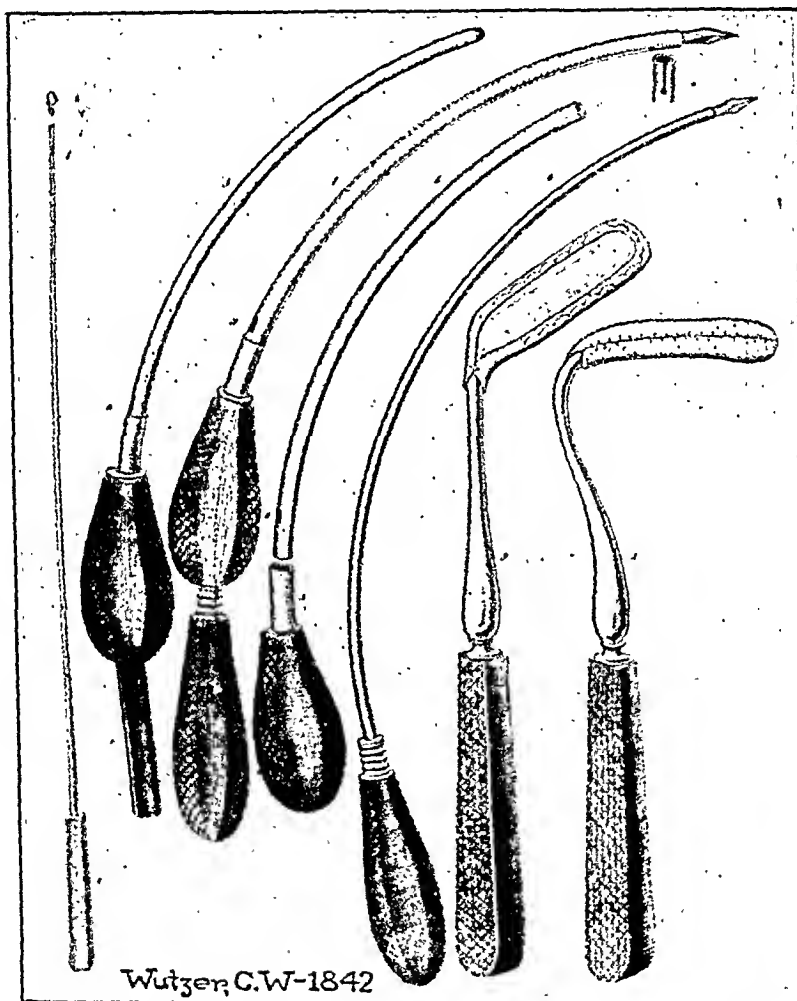


FIG. 4.—Instruments designed by Wutzer. Note trocars used for suprapubic drainage.

that his record has stood the test of time and with few exceptions has never been equaled. The remaining decades of the nineteenth century are studded with reports on the subject, each adding in its own way to the rapid progress which now characterized the treatment of vesicovaginal fistulas.

Fortunately, perhaps for us and for patients afflicted with bladder injuries, so intense did the interest in vesicovaginal fistulas become that there developed a vigorous controversy over the best method of treatment. Leading participants in this controversy were Simon in Germany, and Bozeman<sup>20-24</sup> in this country. The literature of their day is replete with interesting side lights involving these men and their pet methods. Bozeman was tenacious and loyal to his "button"

suture (consisting of silver wire employed in the manner of Sims but held in place by a small perforated lead clamp or "button" through which the wire ends passed) for which he claimed better coaptation of the fistulous edges. The idea was ingenious and in the hands of this remarkable surgeon gave enviable results. Bozeman used a knee-elbow position for his patients when operating, and like most American surgeons of his day laid considerable stress on proper preoperative preparation. This included local hygiene leading to healthier tissue and incision of cicatricial bands to permit mobilization of the fistula. Readers

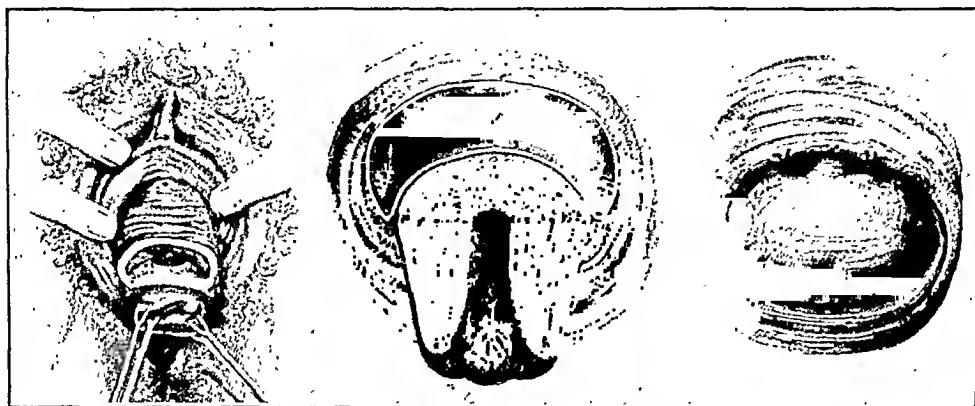


Fig. 5.—Closure of fistula by using cervix as a stop-gap. This technique was used by Jobert de Lamballe in 1852, and is described in his book entitled *Traité des Fistules Vesico-Uterines*.

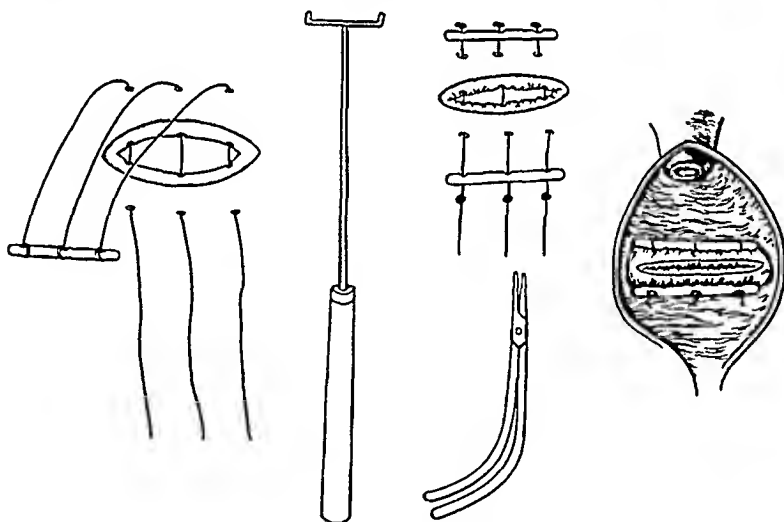


Fig. 6.—The use of wire was not original with Sims, but to him goes the credit of popularizing this method of closure in America.

of medical history may well linger with these masters in the closing years of the nineteenth century, for few surgical developments are illuminated by more interesting side lights.

In 1890 Trendelenburg<sup>146</sup> attempted to repair a vesicovaginal fistula by the suprapubic route. With this new avenue of approach dawned our modern and more versatile era in the treatment of this condition. So intense was the stimulus engendered by the leaders in this type of surgery that in 1906 Kelly<sup>86</sup> was able to report a variety of approaches for the correction of vesicovaginal fistulas including: (A) Parasacral route (Kraske's), (B) ischiorectal route (Michaux), (C) transperitoneal route (Sanger), (D) paravaginal route (Schuehardt's In-

cision), (E) vaginal route (Jobert de Lamballe, Sims, Simon), (F) transvulval or episial route, (G) transurethral route (Kolischer), (H) vestibular route (Jobert de Lamballe), (I) transpubic route (removing a pubic ramus) (Samter), (J) trans-symphyseal route (Bramann, Wickhoff), (K) suprapubic extraperitoneal (Trendelenburg), (L) transvesical, transperitoneal (Von Dittel and others).

Most of the approaches named by Kelly were destined to be short lived or perhaps reserved for selected cases. Only the vaginal, the su-

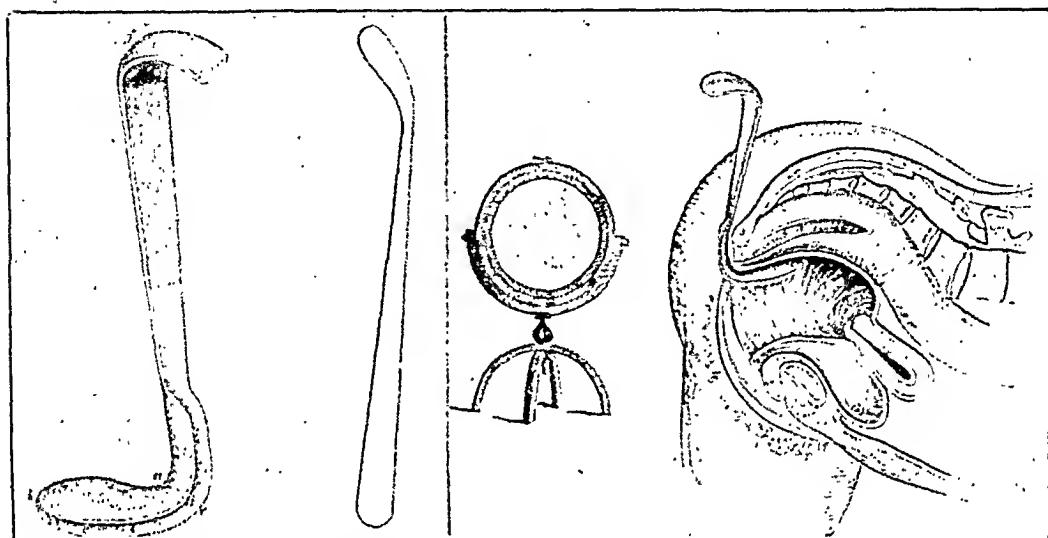


Fig. 7.—Adequate lighting is no longer a major problem, but a century ago it was one of the obstacles to successful treatment. Sims minimized this problem by using reflected sunlight.

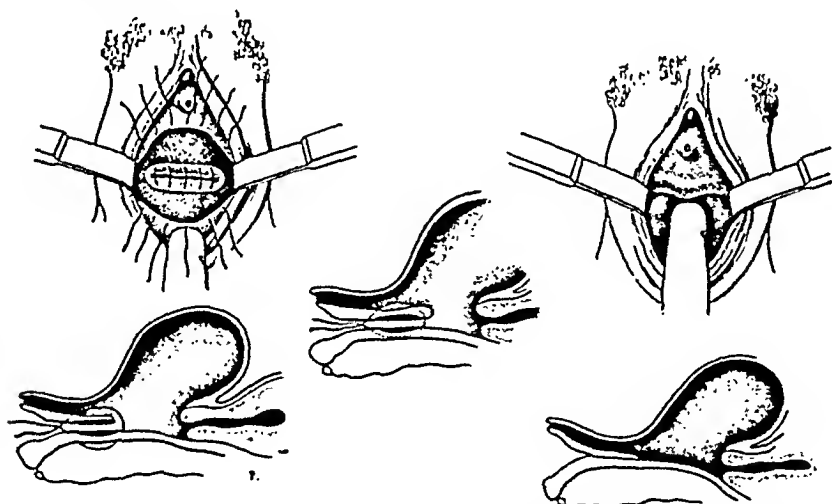


Fig. 8.—Simon, another great leader in the treatment of bladder fistulas, was a contemporary of Sims, Bozeman and Brown. Closure of the vagina as first devised by Maisonneuve was also advocated by Simon. His technic is shown above.

prapubic, transvesical, and transabdominal are accepted today as sound and practicable. Although interest in the suprapubic approach was slow in developing, its progress has been steady, and today we find the transvesical suprapubic approach ranking second in popularity. The gradual favoring of the suprapubic approach may be attributed to the fact that fistulas today are commonly the result of surgical trauma, and

frequently less accessible than those resulting from parturition, especially in cases where total hysterectomy has been performed. Perhaps another reason for the increased interest in the suprapubic route may be found in the fact that urologists are more frequently consulted than in former years.

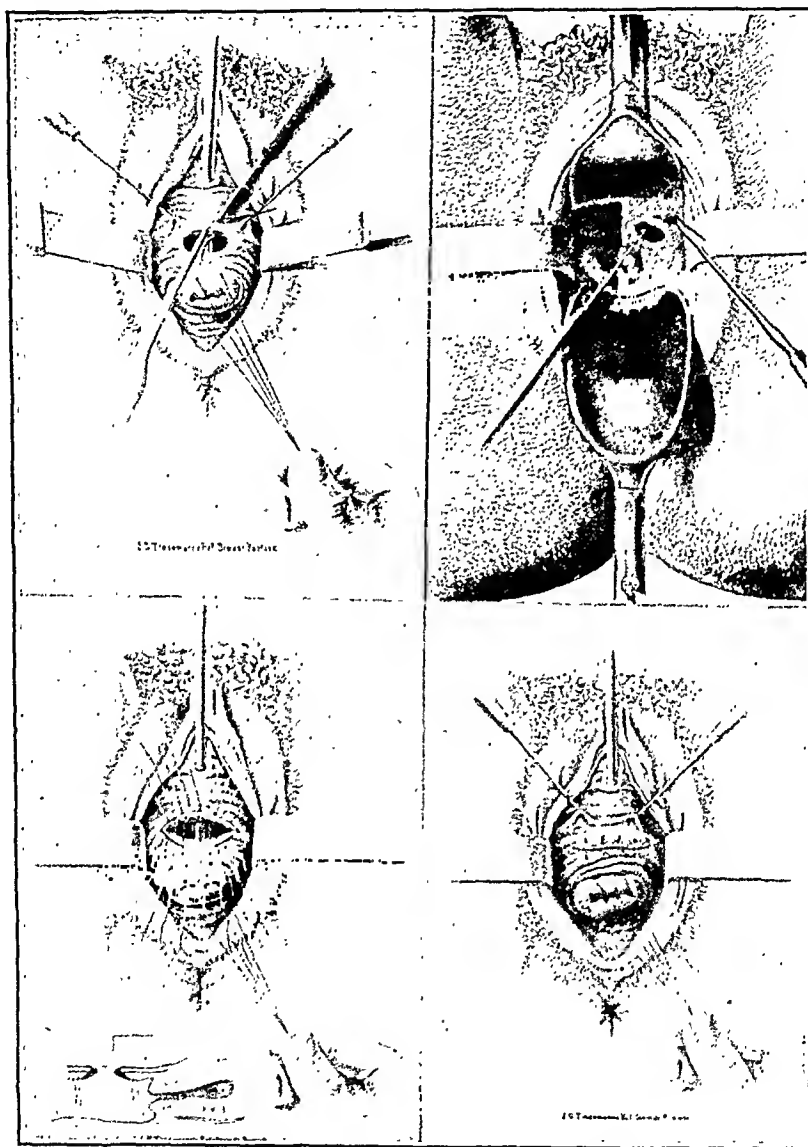


Fig. 9.—Technie used by Simon in repair of bladder fistula as described in his text *Operation der Blasen Scheidenfisteln*.

Revival of the transabdominal route of Sanger and Von Dittel<sup>42, 43</sup> was given a real stimulus by Légueu,<sup>46, 47</sup> who in 1929 reported 89 per cent cures by this approach. The higher mortality connected with this method is a factor to be considered in selecting a suitable technic.

Contemporary treatment of vesicovaginal fistulas may best be characterized by (1) variety of approach, (2) emphasis on mobilization of bladder and vaginal mucous membranes, (3) a general but not unanimous

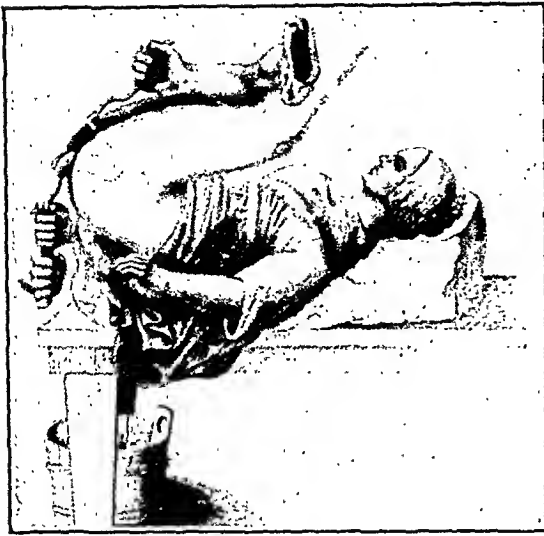
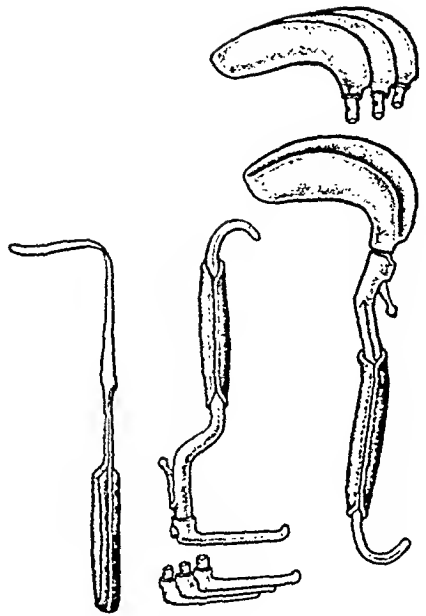


Fig. 10.



Simon 1862

Fig. 11.

Fig. 10.—Simon preferred his patients in the exaggerated lithotomy position when operating for vesicovaginal fistula. This figure taken from an old wood cut portrays the operating room set-up of Simon's time.

Fig. 11.—Like his contemporaries Simon also devised his own instruments. Shown here are the retractors designed and used by him in 1862.

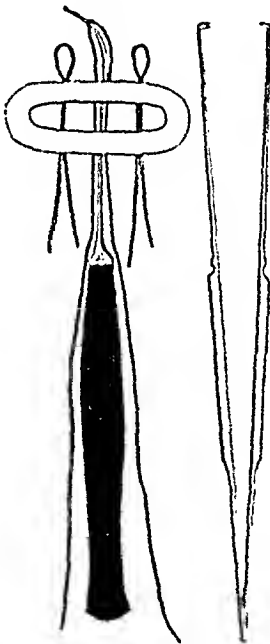
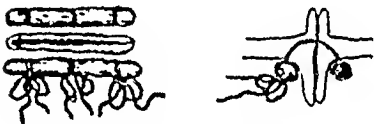


Fig. 12.

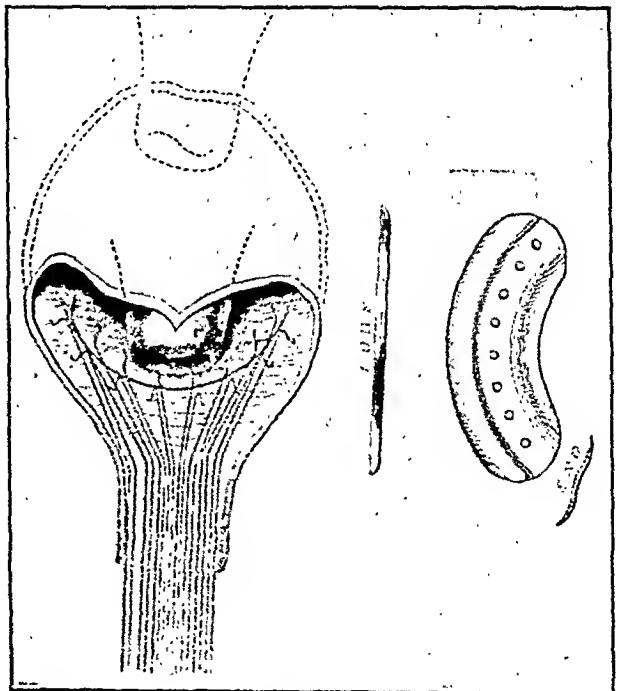


Fig. 13.

Fig. 12.—Technic and instruments used by Maurice H. Collis, Irish surgeon, in the treatment of fistulas.

Fig. 13.—Bozeman, a contemporary of Sims, achieved great success in the treatment of vesicovaginal fistula. Much of this he attributed to the use of so-called "buttons" by means of which he successfully kept the denuded edges of the fistula in close approximation. This figure shows one of these buttons.

trend away from the use of silver wire, and (4) condemnation of col-pocesis. Except for versatility in mode of approach no new stop-gaps

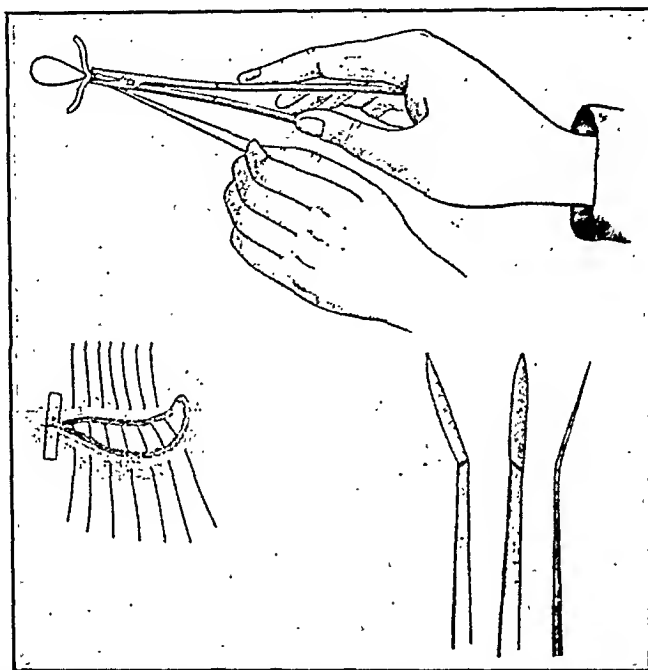


Fig. 14.—Brown, an English contemporary of Sims, Simon and Bozeman, achieved marked success in the treatment of vesicovaginal fistulas. He, too, preferred silver wire and, like many other successful gynecologists, devised many of his own instruments.

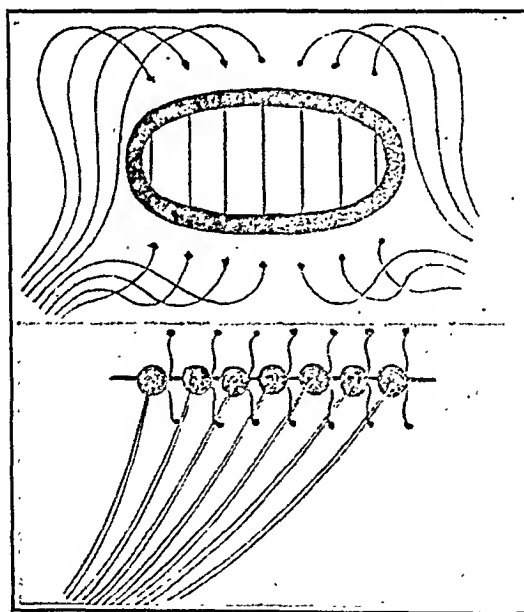


Fig. 15.—Perforated lead shot through which the ends of silver wire were drawn was the usual method of locking the stitches in situ. This is clearly shown in this diagram taken from Agnew.

are recorded. The cervix, uterus, omentum, or musele are still used to cover the opening when there exists no possibility of mobilizing the bladder base sufficiently to close it. In the smaller fistulas, cautery, now,

however, by electrocoagulation, is again being revived with some success. While the new avenues of approach have undoubtedly made possible a cure in many otherwise intractable cases, we cannot overlook the fact that hundreds of fistulas have been cured by operations through the

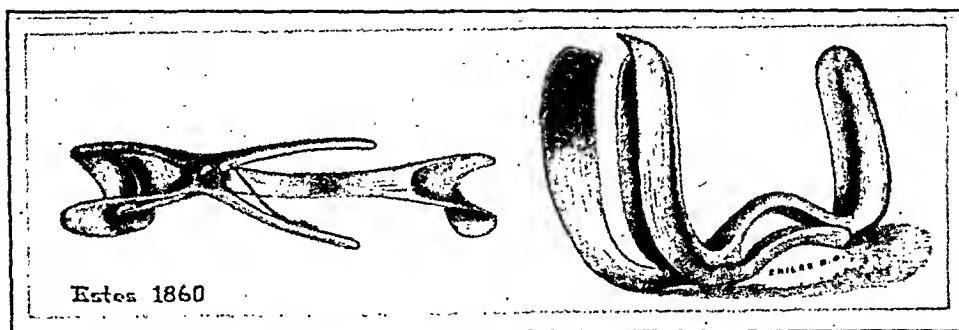


Fig. 16.

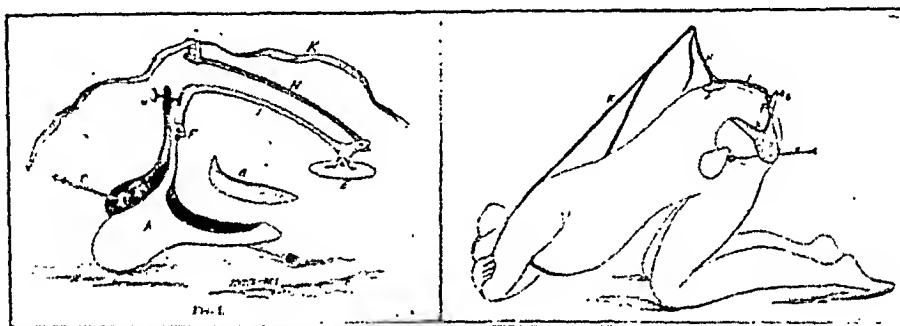


Fig. 17.

Figs. 16 and 17.—Many retractors and speculums were designed to meet the problem of adequate exposure. The self-retaining retractor designed by Erich and the adjustable speculum used by Estes are excellent examples of the ingenuity displayed by the pioneers in this type of work.

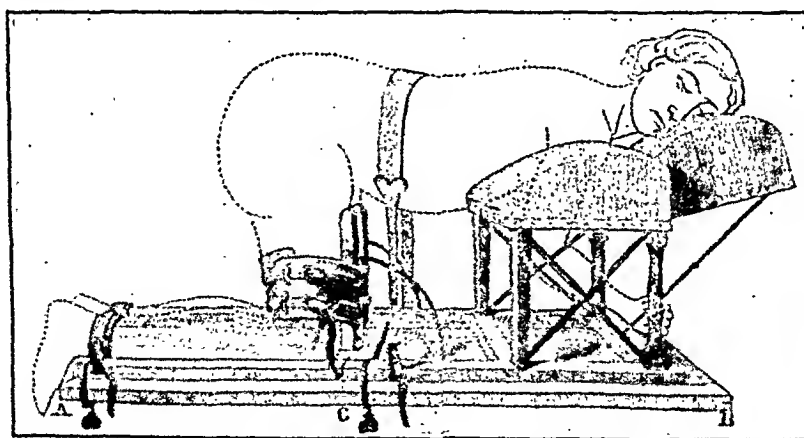


Fig. 18.—Harness and rest used by Bezzeman. Compare with bed and harness designed by Wützer in 1842.

vagina and in all probability this will continue to be the preferred method for a long time to come. Still, it is probably fortunate that both routes are being developed, for there certainly can be no good reason to oppose any safe approach of proved value. The contributions of



Trendelenburg,<sup>146</sup> Meyers,<sup>135</sup> McGill,<sup>135</sup> Thiers,<sup>135</sup> Kelly,<sup>84</sup> Everke,<sup>135</sup> Marion,<sup>135</sup> Young,<sup>160</sup> Sears,<sup>135</sup> and others have shown conclusively that the suprapubic transvesical approach is entirely feasible; and Légeu's<sup>97</sup>

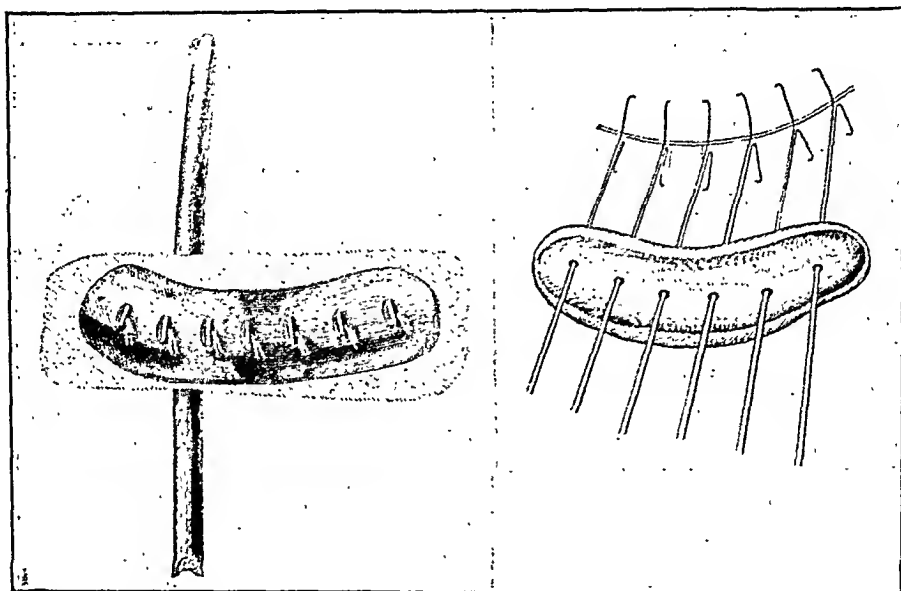


Fig. 19.—"Button" used by Bozeman. Much of his success in treating vesicovaginal fistulas was attributed to their use.

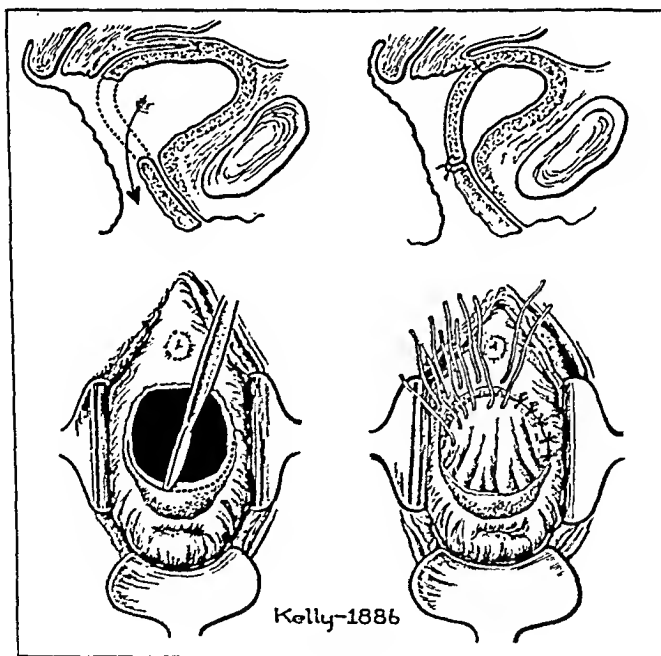


Fig. 20.—Technic used by Kelly in patients with very large fistulas.

technic for the transperitoneal approach may well be considered in selected cases. While my own preference is for the vaginal route, I should have no hesitancy in adopting such other approach as might seem indicated in a given case.

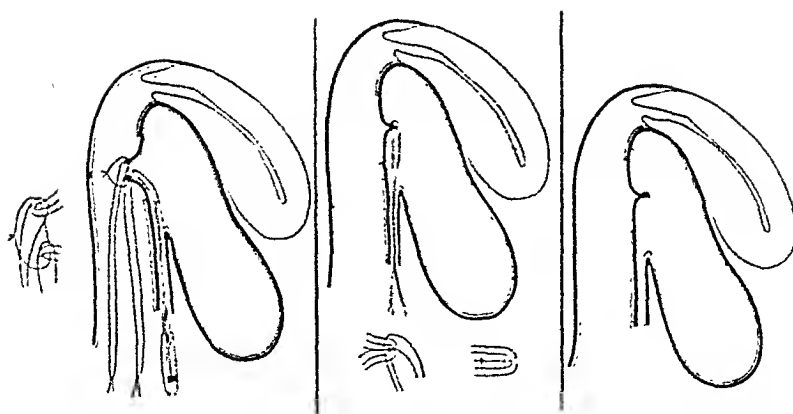
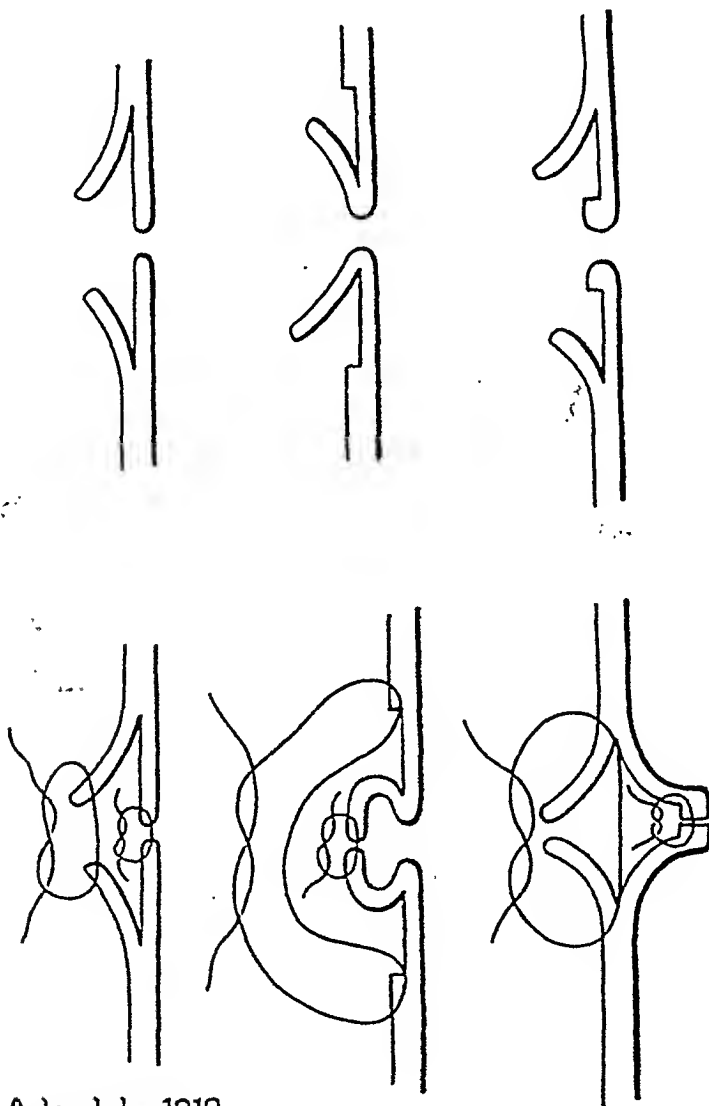


Fig. 21.—Inversion of the edges of the fistula as suggested by Bishop in 1897 sometimes finds advantageous use today.



Adeodata-1919

Fig. 22.—The amount of tissue available often determines how the edges of the fistula shall be treated. Several methods suggested by Adeodata are shown here.

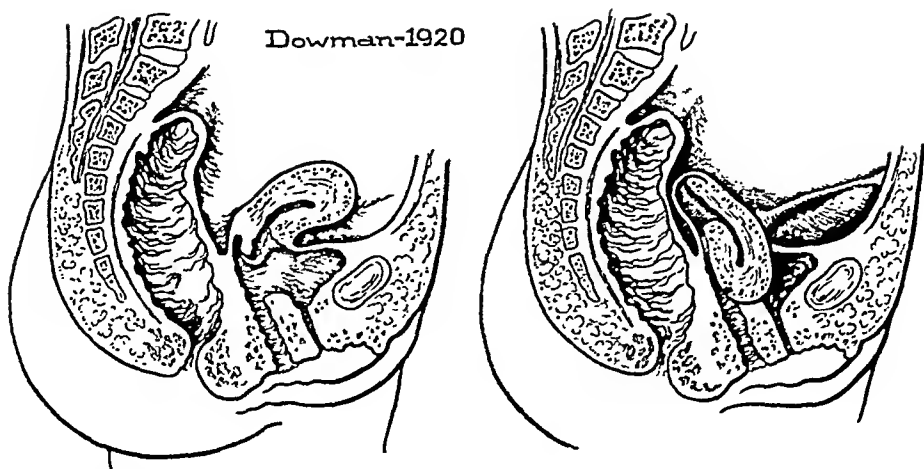


Fig. 23.—Many structures have been used to plug the opening. The cervix was commonly used for this purpose. Use of the uterine body as a stop-gap was suggested by Dowman in 1920.

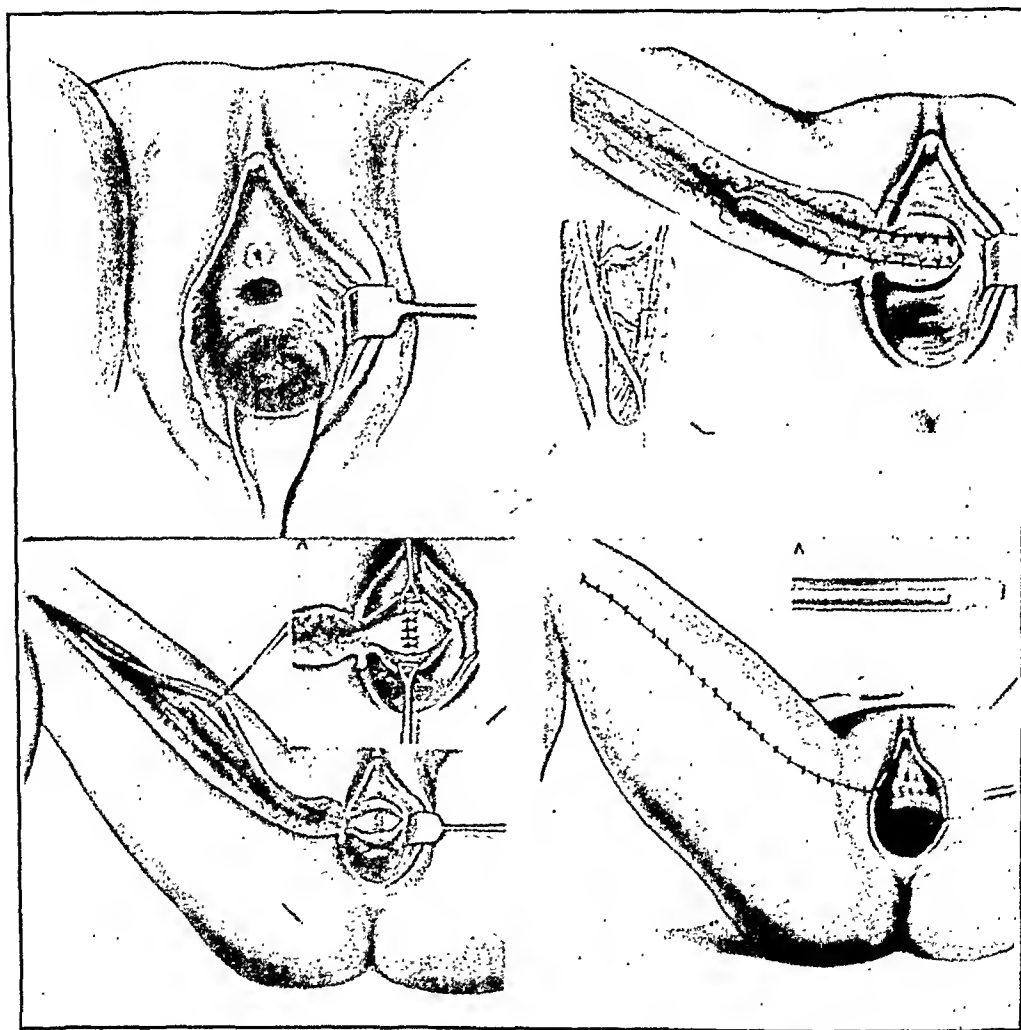


Fig. 24.—Another example of a borrowed stopper is seen in the use of the gracilis muscle as advocated by Garlook in 1928.

Mobilization of the bladder and vaginal mucous membrane has come to be considered a fundamental in present-day treatment. By such methods it is likely that patients have been saved long drawn out preliminary stages when cicatricial bands and scarred areas were prepared for operation. Mobilization is important, for union seldom occurs in the presence of excessive tension. I am not, however, satisfied that the present cry for mobilization is not occasionally over-loud. Slough, resulting from excessive trauma incident to mobilization of badly scarred tissues, with unsuccessful union frequently occurs. Perhaps in cases of excessive scarring, it would be wiser to relieve tension by more remote incisions, leaving the poorly vascularized tissues intact and free from tension. Certainly the results of our illustrious predecessors of the last century have amply demonstrated the practicability of relieving tension in that manner.

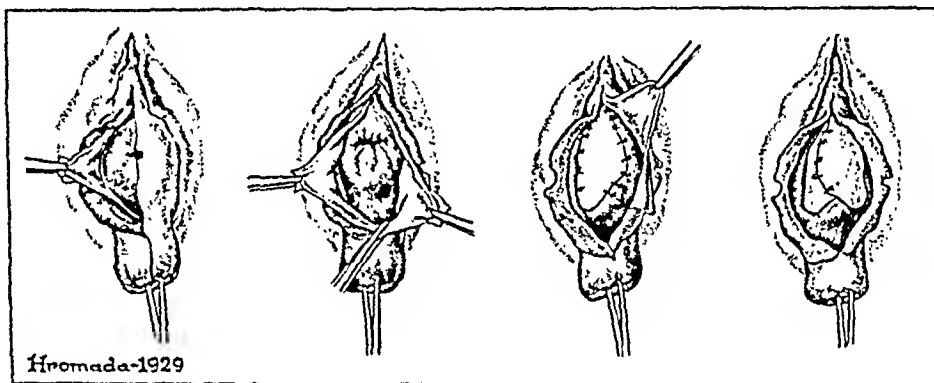


Fig. 25.—Unfortunately the method here shown cannot be utilized readily when the uterus has been removed and the fistula is located high in the vaginal apex.

The trend away from the use of silver wire was natural, paralleling the general use of catgut in other fields of surgery. The wisdom of the change from wire to catgut in the correction of vesicovaginal fistulas has been justly questioned more than once. The almost unparalleled record of Sims, Emmet, Bozeman, staunch advocates of silver wire, scarcely justifies its present consignment to oblivion. Too frequently we do what is being done, never pausing in our acceptance to consider the matter in the light of its true merits. I have never used silver wire and cannot, therefore, speak from experience. It does not appear, however, that the career of catgut as successor to silver wire in the treatment of vesicovaginal fistulas has been characterized by anything remarkable.

Colpocesis or closure of the vagina, first proposed by Vidal, was a real boon to older women with incurable vesicovaginal fistulas. The high or transverse obliteration of the vagina was used by Simon as early as 1856. Opposition to colpocesis was voiced during the late years of the nineteenth century, but its complete elimination probably did not occur until Coffey made his great contribution on ureterointestinal anastomosis.

While we look with intolerance upon colpocesis today, it must be remembered that this was once an operation of inestimable benefit to women with incurable fistulas.

#### STATISTICS

Statistics on the results of treatment in vesicovaginal fistulas are numerous. They range from small series up to 300 and cures rise as high as 95 per cent (Bey). Obviously, however, these results are not

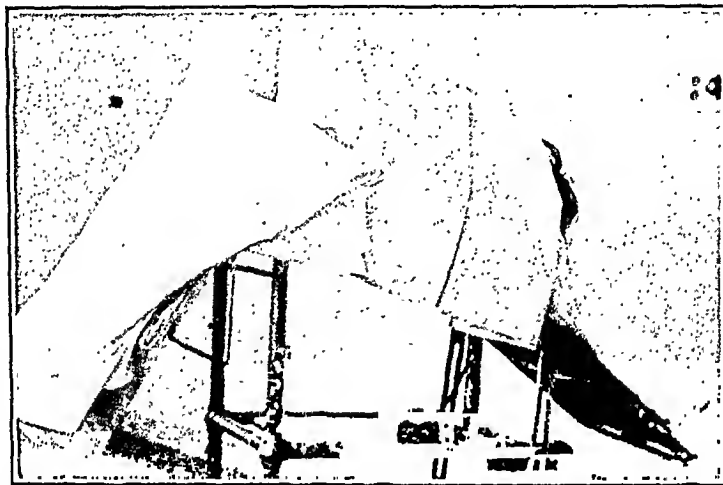


Fig. 26.—With the patient in the inverted Trendelenburg position, good exposure can be obtained by retracting the perineum with a Sims speculum. This permits the operator to look down on the field of operation and tends to minimize technical difficulties.

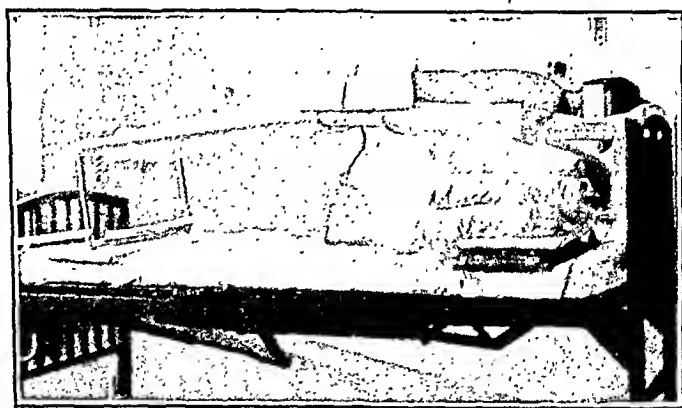


Fig. 27.—When the patient is kept in the prone position following operation, the site of repair is above the urinary pool and gross soiling of the operative site is minimized. Patients are kept in this position for ten days following operation.

easily compared. So many factors must be taken into consideration that one even hesitates to attempt comparisons. In every series the results will depend on certain controllable factors including: (a) skill and technic of the operator, (b) health of tissues, and (c) infection; and upon certain noncontrollable factors as: (a) size of fistulas, (b) location, (c) involvement of other structures, cervix, ureters, urethra, bladder sphincter, etc., and (d) amount of scar tissue. Furthermore

the criteria for cure are not constant and the number of operations necessary to accomplish cure may or may not have been a consideration. The results are often recorded as "satisfactory," an elastic term which may include individuals who, though much improved, still have slight leakage. It would seem that a speedier appraisal of our modern methods of treatment could be achieved were reports to list as cures only those cases where complete healing without leakage obtains. The number of operations required to achieve success should be recorded. Complications should be stated and those involving the urethra, for example, should be listed separately. Certainly cure of the average uncomplicated vesicovaginal fistula is not to be compared with the difficulties encountered in correcting fistulas involving the urethra and bladder sphincter. The statistics given here are by no means complete, but include a sufficient sampling from earlier and present times to permit crude comparison. Space will not permit inclusion of the comprehensive collection of 201 cases (all kinds) reported by Neugebauer in 1891. This interesting compilation is, in a sense, an important historical document covering the problems, operations, and results of the pioneers in the treatment of vesicovaginal fistulas.

## STATISTICS

NAME	YEAR	NO. CASES	ROUTE	CURES	PER CENT
Simon	1854	40	Vaginal	35	87.5
Sims	1860	261	Vaginal	216	82.7
Brown	1863	60	Vaginal	50	83.0
Simon	1869	105	Vaginal	92	89.5
Heppner	1869	22	Vaginal	15	68.0
Emmet	1878	171	Vesico- and recto-vaginal	149	87.1
Toth	1909	131			71.5
Bentall	1910	21			63.0
Frank (Mt. Sinai Hosp.)	1917	19	Vaginal chiefly	14	73.6
Judd (Muyo Clinic)	1920	56	Vaginal chiefly	42	82.0
Mackenzie (Royal Victoria Hosp.)	1922	10	Vaginal chiefly	8	80.0
Schroeder	1922	19	Vaginal chiefly	16	84.0
Saenger (Second Univ. Clinic, Munich)	1929	13	Vaginal chiefly	12	92.3
Sears	1929	50	Transvesical	40	80.0
Léguen	1928	24	Transvesical		64.0
			Transabdominal		89.0
Bey	1929	276	Vaginal chiefly		86.5
Bey	1930	300	Vaginal chiefly		87.0
	Last	100	Vaginal chiefly		95.0
Lower	1930	27	Vaginal chiefly		90.0
Apajalahi (Univ. Clinic)	1931	159	Vaginal chiefly	118	74.0
(Prof. Engstrom Clinic)					
Rawls	1931	149	Vesicovaginal and rectovaginal	86	74.8
Rawls	1934	23	Vaginal	21	91.3

In my own practice a variety of procedures have been tried, from mobilization of bladder and vaginal mucous membranes and approximation, to plugging the opening with the uterus. Since July, 1931, however, a constant method has been used based on the principles that healing is dependent upon:

(1) The presence of healthy tissue (healthy scar tissue included), (2) good blood supply, (3) lack of tension, (4) absence of gross infection, (5) avoidance of gross wetness.

The technic I now use is a composite of many older methods. Briefly, it consists of the following:

*Preparation:* (1) Preoperative preparation: Local hygiene, douches, baths, local application of antiseptics, if necessary. (2) Urinary antisepsis\*: Fluids not forced, ammonium chloride and urotropin each, gr. v. four times daily. (3) Bladder irrigations if indicated. (4) Cystoscopic with localization of ureteral orifices.

If the health of the tissue is good, this preliminary preparation may last but a few days. If, however, the local hygiene is poor, the tissues edematous and the injury recent, the patient may be sent home to carry on as outlined above until at least three months have elapsed since the injury was sustained.

#### *Operation.*—

1. Inverted Trendelenburg position; prone with head down. (In our small series many positions have been tried but this position has always proved most helpful.)

2. Mobilization of bladder and vaginal mucous membranes. (When tissues are badly scarred, trauma and damage to poorly vascularized tissue is lessened by remote mobilization.)

3. Inversion of bladder mucous membranes and eversion of vaginal mucous membranes when possible; twenty-day chromic catgut No. 1 or 0 being used.

#### *Postoperative.*—

1. Prone position on well-padded frame for ten days.

2. Indwelling catheter in bladder with daily boric irrigations. (I am well aware of the divided opinion concerning the use of a catheter for postoperative drainage but feel that no good argument against its use has yet been raised and in our experience it has been of real benefit.)

3. Normal amount of clear fluids only (not forced).

4. Urotropin gr. v, ammonium chloride gr. v, four times daily.

By using this position the repaired wall of the bladder is "on top" and though moisture cannot be prevented, the site of operation at least is not at the bottom of the bladder pool.

### RESULTS

Thirteen consecutive vesicovaginal fistulas, varying in size from pin-point to two inches in length, have been treated in this manner. The last and most difficult was fixed to the left pubic ramus and densely scarred, a case very similar, I believe, to that reported by Phaneuf in 1933.

Most of these fistulas were small, but this is not always a good criterion as to ease of closure. No 13 was particularly difficult because of its location behind the left pubic ramus and the scar tissue, while No. 1 though two inches in length was easy to close.

\*See article, *Miller and Chu: Am. J. Surg.* 23: 457, 1934.

No one familiar with the history of vesicovaginal fistulas and the large series of cases reported by the early masters in this line of work can feel other than humble when venturing to record a small series of thirteen consecutive cases such as I have done here. I am not deluded by the fact that twelve patients have been healed following a single operation in each instance (No. 13 is still convalescent in the hospital) for I know full well that this is a coincidence and that all too soon failures will occur. I sincerely believe, however, that the plan of treatment outlined combines desirable features which favor primary healing.

## SUMMARY OF OPERATIONS BY AUTHOR'S TECHNIC

NO.	SIZE INCHES	COMPLICATION	ETIOLOGY	NO. OF OP- ERATIONS ELSE- WHERE PRIOR TO ADMISSION	NO. HERE	RESULTS
1	2		Parturition	0	1	Cure
2	1/4	Prev. panhysterectomy	Operation	2 cautery	1	Cure
3	1/8	2 1/4-inch fistula vag. apex. Hysterectomy	Operation	0	1	Cure
4	1/4		Operation	0	1	Cure
5	1/4		Parturition	1	1	Cure
6	1/2- 1/8	Radium. Panhysterectomy. Double fistulas far apart. Treated separately at same operation	Operation	0	1	Cure
7	1/4	Panhysterectomy	Operation	2	1	Cure
8	Very small		Parturition	1 oper. 1 cautery	1	Cure
9	1/4		Parturition	0	1	Cure
10	1/4		Parturition	0	1	Cure
11	1/2		Parturition	0	1	Cure
12	Very small	Panhysterectomy	Operation	0	1	Cure
13	1/2	Behind left pubic ramus	Parturition	0	1	Cure

In presenting this subject I have tried to bring to a focus those methods of treatment which appear most practical either by virtue of results produced or soundness of principle or both. By so doing, I may have made it a little easier to fulfill the prerequisites of a successful surgeon in this type of work.

NOTE: Since this paper was read two additional patients have been operated upon, with cure in each case.

## REFERENCES

- (1) *Abadie, J.*: Cong. Franc. de Chir. 29: 549, 1920. (2) *Adeodato, J.*: Brazil med. 33: 273, 1919. (3) *Agnew, D. H.*: Med. & Surg. Rep. 1: 339, 1859. (4) *Idem*: 6: 572, 1861. (5) *Idem*: 15: 1, 57, 115, 190, 272, 309, 328, 373, 391, 413, and 478, 1866. (6) *Allen, T. J.*: New Orleans M. & S. J. 16: 33, 1888. (7) *Ashe, E. O.*: Brit. M. J. 1: 275, 1924. (8) *Assaki*: Ann. d. mal. d.



- org. gen. ur., Par. 14: 1072, 1896. (9) *Bartlett, J. K.*: Trans. Wis. St. M. S. 5: 67, 1871. (10) *Baumm, P.*: Arch. f. Gynäk. 39: 492, 1891. (11) *Bégouin*: Bull. Soc. d'obst. et de gynéc. de Paris 22: 54, 1933. (12) *Bentall, W. C.*: Lancet 2: 796, 1910. (13) *Berger, P.*: Bull. et mém. Soc. de chir. de Paris 23: 142, 1897. (14) *Bey, Mahfouz*: J. Obst. & Gynec. Brit. Emp. 37: 566, 1930. (15) *Bishop, E. S.*: Trans. M. Soc. 20: 123, 1897. (16) *Bissell, Dougal*: Am. J. Surg. 7: 143, 1929. (17) *Bloch, Jacques-Charles*: Médecine 9: 529, 1927. (18) *Bond, C. J.*: Ann. Surg. 20: 392, 1894. (19) *Bonnet, Louis*: Bull. et mém. Soc. de chir. de Paris 20: 673, 1928. (20) *Bozeman, Nathan*: N. A. M. Chir. Rev. 1: 576 and 585, 1857. (21) *Idem*: Med. Rec. 2: 433, 1867. (22) *Idem*: New York M. J. 8: 484, 1869. (23) *Idem*: Am. J. M. Sc. 60: 100, 1870. (24) *Idem*: Internat. J. Surg. 21: 10, 1911. (25) *Brown, I. B.*: Lancet 2: 581, 1859. (26) *Idem*: On Surgical Diseases of Women, ed. 2, London, 1861, J. W. Davies. (27) *Idem*: Obst. Trans. 5: 25, 1863. (28) *Brownson, J. J.*: M. Prog. 67: 174, 1895. (29) *Bruhl, G. C.*: Cincinnati M. Observer 2: 546, 1857. (30) *Caffier, P.*: Ber. ü. d. ges. Gynäk. u. Geburtsh. 27: 593, 1934. (31) *Carstens, J. H.*: Med. Age 3: 126, 1885. (32) *Cassan*: Gaz. d. hôp. 45: 754, 1872. (33) *Caulk, J. E.*: South. M. J. 13: 116, 1920. (34) *Cazin*: Arch. gen. de med. 1: 275 and 436, 1881. (35) *Chacón, Fr. De P.*: Gac. méd. de México 23: 247, 1888. (36) *Child, C. G., Jr.*: Am. J. Obst. 76: 455, 1917. (37) *Chute, A. L.*: J. Urol. 6: 77, 1921. (38) *Collis, M. H.*: Dublin J. M. Sc. 23: 119, 1857. (39) *Croasdale, H. T.*: Boston M. & S. J. 110: 516, 1884. (40) *Delanay, E.*: Paris Chir. 18: 203, 1926. (41) *Dieffenbach, J. F.*: Med. Ztg. 5: 117, 173, 177, 1836. (42) *von Dittel*: Med. Jahrb. p. 563, 1881. (43) *Idem*: Wien. klin. Wehnschr. 6: 449, 1893. (44) *Döderlein, A.*: Ztschr. f. Urol. 23: 453, 1929. (45) *Dowman, C. E.*: Surg. Gynec. Obst. 30: 403, 1920. (46) *Dudley, E. T.*: Nashville, Am. J. Surg. & Gynec. 12: 169, 1898/99. (47) *Duplay*: Gaz. méd. de France 59: 85, 1888. (48) *Eastman, J. R.*: J. Indiana M. A. 13: 393, 1920. (49) *Ehrendörfer*: Wien. klin. Wehnschr. 11: 527, 1898. (50) *Emmet, T. A.*: Vesico-vaginal Fistula From Parturition and Other Causes; With Cases of Recto-vaginal Fistula, New York, 1868, W. Wood & Co. (51) *Idem*: Tr. Am. Gynec. Soc. 3: 114, 1878. (52) *Idem*: Am. J. Obst. 31: 593, 1895. (53) *Erich, A. F.*: New York M. J. 8: 478, 1869. (54) *Estes, H.*: New Orleans M. & S. J. 17: 792, 1860. (55) *Eve, P. F.*: Gaz. méd. de France 11: 166, 1860. (56) *Farman, Franklin, and Thompson, E. C.*: J. Urol. 20: 663, 1928. (57) *Flaischlen, Nicolaus*: Zentralbl. f. Gynäk. 19: 1086, 1895. (58) *Frankel, L.*: Zentralbl. f. Gynäk. 48: 2562, 1924. (59) *Frank, R. T.*: AM. J. OBST. & GYNEC. 24: 411, 1932. (60) *Freund, R.*: Chirurg. 1: 205, 1928/29. (61) *Garfunkel, Paul*: Zentralbl. f. Gynäk. 49: 2307, 1925. (62) *Garlock, J. A.*: Surg. Gynec. Obst. 47: 255, 1928. (63) *Gayet*: Lyon Chir. 29: 119, 1931. (64) *Goodell, William*: Am. J. Obst. 16: 742, 1883. (65) *Gosset, J.*: Lancet 1: 345, 1834. (66) *Graff, E.*: Wien. klin. Wehnschr. 75: 2392, 1925. (67) *Graham, H.*: Lancet 1: 228, 1841. (68) *Greene, W. W.*: M. Rec. 1: 465, 1866. (69) *Halban, J.*: Zentralbl. f. Bakteriöl. 47: 588, 1923. (70) *Hanks, H. T.*: Internat. J. Surg. & Antisept. 1: 132, 1888. (71) *Heppner, C. L.*: Monatschr. f. Geburtsh. u. Frauenkr. 33: 95, 1869. (72) *Herrgott*: Rev. de chir. Par. 4: 574, 1884. (73) *Hirst, C. B.*: Ann. Gynec. & Pediat. 4: 365, 1890/91. (74) *Hromada, Gebhard*: Zentralbl. f. Gynäk. 53: 1431, 1929. (75) *Jacoby, M.*: Ztschr. f. Urol. 25: 529, 1931. (76) *Jobert, A. J.*: Gaz. d. hôp. 8: 405 and 437, 1834. (77) *Jobert, A. J.*: Bull. Acad. Roy. de méd., Paris 2: 581, 1837/38. (78) *Idem*: Traité des fistules vesico-utérines, Paris, 1852, J. B. Baillière. (79) *Idem*: Gaz. d. hôp. 8: 405 and 437, 1854. (80) *Judd, E. S.*: Surg. Gynec. Obst. 30: 447, 1920. (81) *Judd, E. S., and Waldron, G. W.*: S. Clin. J. N. A. 14: 551, 1934. (82) *Kahn, Emanuel*: Zentralbl. f. Gynäk. 23: 198, 1899. (83) *Keller, R.*: Arch. franco-belges de chir. 33: 568, 1932. (84) *Kelly, H. A.*: Bull. Johns Hopkins Hosp. 7: 29, 1896. (85) *Idem*: 10: 115, 1899. (86) *Idem*: Tr. Am. Gynec. Soc. 31: 225, 1906. (87) *Idem*: 37: 3, 1912. (88) *Kerr, J. M. M.*: Proc. Roy. Soc. Med. 14: 193, 1920/21. (89) *Kleefisch, Johannes*: Zentralbl. f. Gynäk. 54: 258, 1930. (90) *Klumper, P.*: Nederl. tijdschr. v. Geneesk. 2: 674, 1922. (91) *Kolischer, Gustav*: Wien. med. Presse 38: 1630, 1897. (92) *Kolischer, Gustav, and Jones, A. E.*: Urol. & Cutan. Rev. 29: 593, 1925. (93) *Kulenkampf, D.*: Zentralbl. f. Gynäk. 51: 1909, 1927. (94) *Latzko, W.*: Wien. klin. Wehnschr. 44: 103, 1931. (95) *Idem*: Zentralbl. f. Gynäk. 57: 1026, 1933. (96) *Léguen, F.*: Gynécologie 27: 385, 1928. (97) *Idem*: Surg. Gynec. Obst. 48: 796, 1929. (98) *Lower, W. E.*: Tr. Am. Surg. Assn. 48: 336, 1930. (99) *Idem*: J. Urol. 26: 141, 1931. (100) *McGill, A. F.*: Lancet 2: 966, 1890. (101) *McGlinn, J. A.*: AM. J. OBST. & GYNEC. 24: 262, 1932. (102) *Mackenrodt, A.*: Zentralbl. f. Gynäk.

- 18: 180, 1894. (103) *Idem*: Monatschr. f. Geburtsh. u. Gynäk. 5: 445, 1897. (104) *Madden, T. M.*: M. Press & Circ. 43: 545, 1887. (105) *Mandelstamm, A.*: Zentralbl. f. Gynäk. 56: 334, 1932. (106) *Mann, M. D.*: Internat. M. Mag. 2: 547, 1893/94. (107) *Marion*: An. de l'ac. de med., Montevideo 4: 765, 1919. (108) *Martin, A.*: Ztschr. f. Geburtsh. u. Gynäk. 19: 394, 1890. (109) *Martius, H.*: Ztschr. f. Geburtsh. u. Gynäk. 103: 22, 1932. (110) *Mayo, C. H.*: Ann. Surg. 63: 106, 1916. (111) *Mayo, C. H., and Walters, W.*: Surg. Clin. N. A. 4: 399, 1924. (112) *Meriel, E.*: Gynécologie 27: 467, 1928. (113) *Miller, C. J.*: New Orleans M. & S. J. 82: 850, 1929/30. (114) *Müller, G.*: Časop. lék. česk. p. 1357, 1925. (115) *Naegeli, T.*: Deutsche Ztschr. f. Chir. 200: 445, 1927. (116) *Neugebauer, F. L.*: Arch. f. Gynäk. 33: 270, 1888; 34: 143, 1889; 35: 257, 1889; 39: 508, 1891. (117) *Nicodemi, Cesare*: Riforma med. 2: 73, 1898. (118) *Noble, C. P.*: AM. J. OBST. & GYNEC. 13: 395, 1898. (119) *Ottow, B.*: Zentralbl. f. Gynäk. 51: 349, 1927. (120) *Idem*: 53: 1444, 1929. (121) *Paine, H. S.*: Albany M. Ann. 9: 65, 1888. (122) *Parvin, Theophilus*: M. Rec. 1: 321, 1866. (123) *Peterson, Anders*: Am. J. Surg. 17: 247, 1932. (124) *Phaneuf, L. E.*: Am. J. Surg. 19: 29, 1933. (125) *Rawls, R. M.*: Curtis' Obstetrics and Gynecology 3: Chapter LXXXII, Philadelphia, 1933, W. B. Saunders Co. (126) *Richard*: Bull. et mém. Soc. de chir. de Paris 26: 258, 1900. (127) *Roeder, C. A.*: Surg. Gynec. Obst. 45: 102, 1927. (128) *Rübsamen, W.*: Arch. f. klin. Chir. 118: 220, 1921. (129) *Routier, M.*: Bull. et mém. Soc. de chir. de Paris 23: 90, 1897. (130) *Ryan, Michael*: London Med. J. 6: No. 144, 1834. (131) *Samter, O.*: Zentralbl. f. Chir. 59: 1734, 1932. (132) *Schauta, F.*: Monatschr. f. Gynäk. 1: 8, 1895. (133) *Schroeder, E.*: Monatschr. f. Geburtsh. u. Gynäk. 23: 60 and 129, 1922. (134) *Scudder, Ida*: Tr. Seventh Cong. Far East Assn. Trop. Med. 1: 355, 1927. (135) *Sears, N. P.*: AM. J. OBST. & GYNEC. 18: 267, 1929. (136) *Seitz, L.*: Arch. f. Gynäk. 142: 74, 1930. (137) *Simon, Gustav*: Monatschr. f. Gynäk. 12: 42, 1858. (138) *Idem*: Operation der Blasenscheidenfisteln, Rostock, Stiller's Hofbuchhandlung, 1862. (139) *Idem*: AM. J. OBST. & GYNEC. 2: 232, 1869. (140) *Sims, H. M.*: New York J. Gynec. 3: 415, 1893. (141) *Sims, J. M.*: Am. J. M. Sc. 23: 59, 1852. (142) *Spencer, R.*: Tr. Am. Gynec. Soc. 50: 110, 1925. (143) *Stranach, P.*: Cor.-Bl. D. allg. ärztl. Ver. v. Thüringen 20: 137, 1891. (144) *Suchon, Edmund*: New Orleans M. & S. J. 15: 194, 1887/88. (145) *Tait, Lawson*: Dublin J. M. Sc. 85: 381, 1888. (146) *Trendelenberg, Friedrich*: Samml. Klin. Vortr., No. 355, 1890. (147) *Trombetta, Francesco*: Gior. internat. d. sc. med. 5: 829, 1883. (148) *Turenne, Augusto*: Assoc. Med. Arg. Rev. 29: 95, 1918. (149) *Vance, R. A.*: Cleveland M. Gaz. 3: 135 and 175, 1888. (150) *Vitrac*: Gaz. hebdom. 4: 1190, 1899. (151) *Vogt, E.*: Zentralbl. f. Gynäk. 56: 1105, 1932. (152) *Ward, G. J.*: Surg. Gynec. Obst. 25: 126, 1917. (153) *Watkins, T. J.*: Surg. Gynec. Obst. 40: 274, 1925. (154) *Webb, M. V.*: Tr. Seventh Cong. Far East Assn. Trop. Med. 1: 351, 1927. (155) *von Winckel*: Ztschr. f. Geburtsh. u. Gynäk. 30: 463, 1894. (156) *Wilkerson, T. B.*: N. Car. M. J. 12: 315, 1883. (157) *Wisniewski, F. F.*: Ill. M. S. 51: 483, 1927. (158) *Wützer, C. W.*: Org. f. d. ges. Heilk. 2: 469, 1842. (159) *Idem*: Deutsche Klin. 1: 32 and 43, 1849. (160) *Young, H. H.*: Surg. Gynec. Obst. 45: 226, 1927. (161) *Zangemeister, W.*: Zentralbl. f. Gynäk. 53: 352, 1929.

---

Bagetti, Mario: Lipoma of the Fallopian Tube, La Ginecologia 2: 211, 1935.

Emphasizing that primary benign tumors of the fallopian tubes are not uncommon, the author describes a case of lipoma of the tube, found in a thirty-eight-year-old woman during an operation.

Lipoma of the fallopian tubes is rare. More importance is attached to the anatomicopathologic interest than the clinical. This newgrowth represents an accidental finding during a surgical intervention or at autopsy. The growth has no specific symptomatology.

AUGUST F. DARO.

## TUBAL REIMPLANTATION—IN RETROSPECT\*

GEORGE DE TARNOWSKY, M.D., F.A.C.S., CHICAGO, ILL.

(From the University of Illinois School of Medicine and Ravenswood Hospital)

IN JUNE, 1934, L. E. Bureh published an article on sterilization of the female in which he made the statement that "there is no absolute surgical method of producing sterilization in 100 per cent of cases." It is my desire to challenge this statement and to present, for the second time before this society, a method called tubal reimplantation which I devised in 1911. Four desiderata were uppermost in my mind in devising this procedure:

1. It must be uniformly successful
2. It must not interfere with the physiologic function of the oviducts
3. It must not unsex the women, i.e., neither ovulation nor libido should be interfered with
4. It must be susceptible of reconstruction, i.e., the continuity of both fallopian tubes to the uterine cavity should be capable of restoration

The first three postulates have been completely attained. No intra- or extrauterine pregnancies have supervened; no case of hydrosalpinx has occurred in any of the sixty cases which form the basis of my report and, finally, ovulation and libido have remained normal. To date none of these patients has evinced any desire to court pregnancy; no attempt at reconstruction of the severed tubes has been possible.

In addition to the four principal desiderata, the operation should be a comparatively simple one, carrying with it, per se, no danger to life nor serious incidence of morbidity, and the approach to the tubes should be such as to enable the surgeon to correct any intra-abdominal lesions which might be present.

Twenty-four years ago, when contraceptive methods were hesitatingly suggested by our profession, the *raison d'être* for sterilization was narrowly restricted. Chronic cardiac lesions, active tuberculosis, nephritis, diabetes, and hereditary insanity usually covered the list of nondebatable indications. DeLee taught that any disease which was a contraindication to pregnancy was an indication for sterilization. Curtis<sup>22</sup> lays down the following conventional postulates for sterilization:

1. All those indications for therapeutic abortion which are based upon prolonged or permanent pathologic conditions
2. Repeated hyperemesis gravidarum in the same patient

---

\*Read at a meeting of the Chicago Gynecological Society, May 17, 1935.

3. Chronic renal disease
4. Permanent cardiac lesions with decompression
5. Repeated cesarean section
6. Active tuberculosis
7. Dementia precox
8. Uterine prolapse requiring the interposition operation or ventrofixation
9. Eugenic sterilization

We are in full agreement with all of these indications.

When tubal reimplantation was discussed before the Chicago Gynecological Society in 1913 four cases were reported. Two of the patients had active tuberculosis, the third was a multipara suffering from chronic nephritis who developed eclampsia at the time of her last parturition, and the fourth a multipara who, following a ventral suspension for prolapsus, became pregnant. She developed such marked pelvic disturbances that intervention was suggested and accepted. The adhesions encountered were so dense and extensive that it was deemed best to sterilize the patient and empty the uterus.

No sterilizations should be performed on unmarried girls unless marriage is contemplated in spite of clearly demonstrable contraindications to pregnancy. With Burch, I believe that sterilization should not be carried out unless contraceptive measures have failed, create esthetic disgust in the mind of one or both partners, or where both parties will not cooperate in their use. Vasectomy is accepted by a few husbands, strongly objected to by many.

In this present day and age, with the joint consent of both husband and wife, tubal sterilization can and should be offered in lieu of contraceptives or mathematical attempts to determine the so-called "safe period." Both are open to the unquestioned objection that they are not infallible and that they tend to destroy the romance of union. This statement is made in all seriousness and should not be misconstrued. Question either husband or wife sympathetically and tactfully; one will be much enlightened by their expressions of regret or disgust that cohabitation should have become such a prearranged and mechanicochemical procedure.

The almost innumerable methods of female sterilization may conveniently be grouped as follows:

1. Mutilating operations:
  - Hysterectomy
  - Bilateral ovariectomy
  - Bilateral salpingectomy
2. Crushing and ligation of tubes (Madlener, etc.)
3. Tubal knotting (Flatau)
4. Electrocoagulation of the isthmial portion of the tubes
  - Vaginouterine route (Dickinson, Hyams, etc.)
  - Abdominal route (Scheffzek)

5. Plastic operations on the tubes:
  - On the uterine end of the tube
  - On the fimbriated end of the tube
  - Broad ligament infolding of the tube
6. Vaginal route (Heaney, Falls, etc.)
  - Crushing and ligation
  - Partial or complete salpingectomy
7. Incaeceration of both ovaries in broad ligament pockets.

The fallopian tubes may be considered to represent the excretory ducts of the ovaries. That the tubes are lined by both columnar and ciliated epithelium continuous with the uterine mucosa; that mucous membranes secrete and excrete, and that there is a more or less constant directing action of the tubal current produced in the peritoneal fluid by the movements of the cilia on the tubal fimbriae, especially on the fimbria ovarica, is of common knowledge. There is some difference of opinion as to the relative importance of tubal peristalsis and ciliary movement, probably both are equally concerned. The important point to stress is that the oviducts are secreting tubes requiring an outlet yet, so far as one can determine from close perusal of the literature, only two of the many operations described provide for uninterrupted tubal drainage, namely the one devised by Carey Culbertson<sup>7</sup> and by me. Culbertson, attacking the problem from the distal end of both tubes, makes stab wounds in the broad ligament through which he draws the fimbriated ends of the tubes, anchoring them to the anterior culdesac. By suspending the uterus in anteversion and suturing the broad ligament to the parietal peritoneum he completely shuts off the fimbriated ends of both tubes from the pelvic cavity. Physiologic drainage of the tubes is not interfered with. When N. Sproat Heaney, at a recent meeting of the Chicago Gynecological Society, was describing the occurrence of a tubal prolapse following vaginal hysterectomy, it was interesting to have him state that there was a profuse watery discharge from the prolapsed tube into the vagina.

Vignes and Barron,<sup>21</sup> in an experimental study on the regeneration of resected and ligated tubes, reported the constant formation of an aseptic hydrosalpinx which distended the tubes and perhaps aided in their regeneration. It would seem logical to infer that reported failures of the Madlener procedure might be explained on the same basis. Culbertson makes the pertinent statement that "in all operations which permanently close the distal stumps of the tubes the possibility of hydrosalpinx must be considered."

Aldridge<sup>3</sup> used a method somewhat similar in principle to that of Culbertson but, instead of shutting off the anterior culdesac from the rest of the pelvic cavity he made a pocket between the peritoneal folds of the broad ligament and sutured the fimbriated ends of both tubes in these pockets. He reports one case in which the patient, five years after sterilization, requested a freeing of her tubes. This was followed by pregnancy and delivery.

Section and ligation of the tubes, closure of the cornua and burial of the distal stumps in pockets have been carried out by many pelvic surgeons.

Slemons<sup>4</sup> excises the proximal ends of both tubes and implants them in the uterine muscle. A stab wound is made 1 cm. deep either on the anterior or posterior wall of the uterus; the severed ends of both tubes are buried in these pockets and sutured in place. The uterotubal angle is closed in the usual manner. No tubal drainage is possible in this type of operation.

Jackson<sup>25</sup> slits the serosa from the uterine cornua outward for a distance of 4 cm., picks up the denuded portion of tube, and resects the denuded portion, ligating both ends. The broad ligament is whipped over the intervening space with a running whip stitch of linen. His object is to interpose 4 cm. of scar tissue between the ligated stumps. Again, no drainage is provided for the distal portion of the tubes.

Scheffzek<sup>5</sup> destroys the interstitial portion of the tubes as well as their lateral portion. Through a Pfannenstiel incision the abdomen is opened, the tubes are severed transversely at their uterine junction. A thin electric needle is then introduced into the lumen of the tubes and their interstitial portions destroyed down into the uterine cavity. The needle is then introduced into the lateral portion of the tubes and the entire canal is destroyed. There can be little doubt regarding the efficacy of Scheffzek's method. The fact that this method of sterilization was used on insane women may account for its destructive thoroughness. A double salpingectomy would seem to be a much simpler procedure.

Burial of the severed and ligated distal stumps in the broad ligament or in the inguinal canal as practiced by Crossen, Irving, and others may provide for a certain amount of drainage if the ligature is digested before scar tissue closes the tube.

Tubal knotting, practiced by Flatau, jeopardizes the circulation of the tubes and should be unreservedly condemned.

Burial of both ovaries in pockets prepared on the anterior or posterior surfaces of the broad ligament result, in a certain percentage of cases, either in the occurrence of a persistent fistula at the point where the ovarian pedicle enters the broad ligament pocket, or if the sutures around the pedicles are too tight, ovarian atrophy, and amenorrhea result.

The Dickinson and Hyams<sup>6</sup> cauterization provides no tubal drainage unless a reverse peristalsis is established; furthermore, the method is uncertain in its results. Hyams states that "in an occasional case it may be necessary to repeat the procedure. After one month the end-result is determined by transuterine insufflation or utero-salpingography. Distortion of the uterine cavity by fibroids may render electro-coagulation of the tubes difficult or impossible."

Naujocks<sup>8</sup> proposed a "reversible" (temporary) sterilization of the female by crushing the fallopian tubes. He crushes both ampullas for a distance of at least 1 cm., care being taken to include both muscle and mucosa. One must be sure, he states, that, although the tube is crushed, it is not cut or torn. It is then doubly ligated at each end of the crushed area with some nonabsorbable material. The method is advantageous because it is quick, simple, and bloodless, and because it is easily reversible at a late date by simply cutting the tube between the proximal ligature and the uterus, either with a knife or an endotherm cautery. To date Naujocks has no reported any "reversals." Theoretically, one must admit the probability of sloughing of the crushed and ligated fimbriated ends occurring, with restoration of tubal patency.

Rubovits and Kobak<sup>9</sup> recently reported two failures of the Madlener technic. Fuchs<sup>10</sup> examined twelve Madlener types of sterilization and found five of them to be failures anatomically and functionally. Wolff reported that eight of his Madlener operations were functional failures because the lipiodol passed the point of crushing and was visualized up to the fimbriated ends of the tubes.

The vaginal route, advocated by Falls, Heaney, and others, usually involves complete peritonization of the distal stump of both tubes, either against the anterior wall of the uterus or by bringing the round and broad ligaments over the stumps and uterine cornua wounds at the same time, thus peritonizing the entire field of operation. Tubal drainage is not provided for.

Rosenberg<sup>11</sup> reports a case of left tubal pregnancy six months after performing a modified Pomeroy sterilization. Through an anterior colporrhaphy he ligated and resected a large loop of the cornual ends of both tubes and followed this by electrocoagulation of the severed ends of the tubes. His case, and other similar ones, would seem to prove that, unless tubal drainage is directed away from the cornua, failures will occur.

As illustrating the extremes to which gynecologists have been put in attempting to elaborate a uniformly successful method of sterilization, one may mention, en passant, the method of Zomakion, Haendly and Polan which involves the plastic construction of a double vagina, the anterior, smaller tube for menstruation and cervical drainage, the larger, posterior one for coitus.

Equally fantastic is Baskin's<sup>22</sup> temporary sterilization by the injection of human spermatozoa. From 2 to 5 c.c. of semen to which has been added 1 c.c. of hexylresorcinol is injected in the wife's buttock. Three injections, one week apart, are given. One week after the last injection the woman's serum is tested and similar tests are run every three months. Baskin claims a sterilization of one year's duration following this technic.

The steps of the tubal reimplantation as originally described,<sup>1</sup> are as follows (Figs 1, 2, and 3):

1. Through a four-inch-long paramedian incision the pelvic cavity is opened, its contents inspected and any subacute or chronic changes, including the appendix, are attended to primarily.

2. The fundus uteri is grasped with vulsellum forceps and drawn up through the incision.

3. Amputate the tubes one-fourth inch from the cornua. With a fine rat-tooth forceps or a probe, invaginate the cornual stumps and close the lumen with two catgut sutures. Seroserous coaptation must be complete and firm. It will be occasionally necessary to use a portion of uterine wall to complete the cornual invagination.

4. On the posterior uterine wall and close to its fundus make two parallel vertical incisions one inch long and one-half inch apart. These incisions should not be over one-fourth to one-fifth of an inch deep. With a curved forceps gently burrow between the two parallel incisions, thus creating a canal of sufficient size to contain both tubes.

5. With the same curved forceps remaining in the canal, grasp the opposite tube and draw it through the canal so that it emerges on the opposite side; reverse the forceps and repeat the same procedure with the remaining tube. In the new canal the tubes should parallel each other, one lying above the other, the eut extremity of each tube emerging on the opposite side of the canal.

6. Make a small cuff by everting the tubal mucosa (it is sometimes necessary to make two small incisions before being able to evert satisfactorily) and secure the

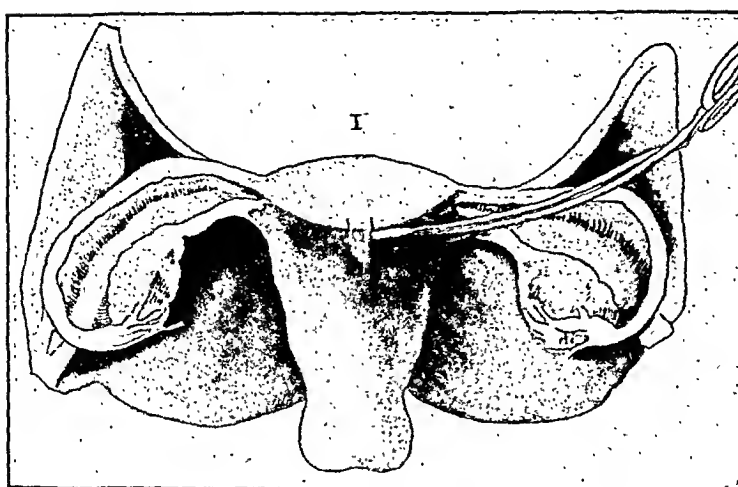


Fig 1.

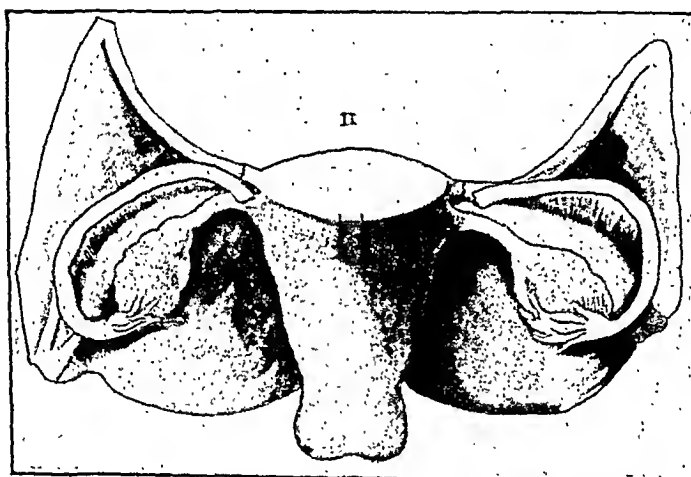


Fig. 2.

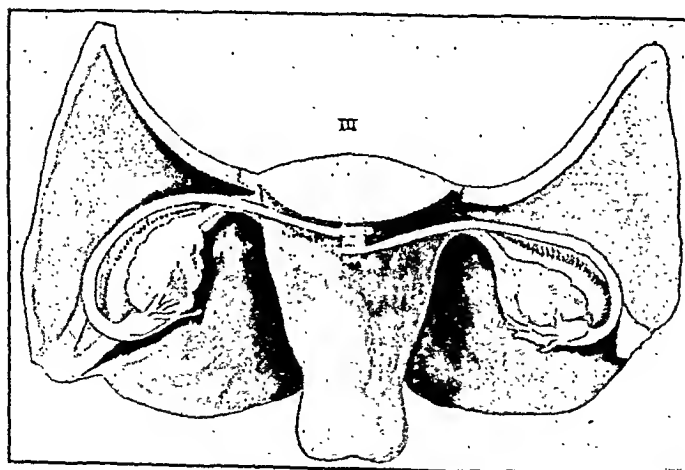


Fig. 3.



cuffs to the margin of the canal by fine catgut sutures which at the same time control any uterine wall oozing which may be present. Test the patency of both tubes by means of a fine probe.

7. Close the abdominal incision in the usual manner.

The only modification in the original technic consists in omitting eversion of the distal ends of the reimplanted tubes. By simply applying two fine catgut stitches uniting each tubal end to the slit or canal in the posterior wall of the uterus, the mucosa is seen to roll outwardly thus preventing tubal closure by adhesions. Where the tubes are unusually small in caliber, a circular portion of uterine wall is included in the cornual excision. This makes a rosette-like stump which is easier to suture in place. There is ample clinical evidence that these tubes remain patent and that the tubal ciliated epithelium continues to function normally. Repeated examinations of sterilized patients have failed to reveal any tubal enlargements. That the ovaries of these patients continue to function normally up to the average climacteric age is amply proved by the follow-up of sixty private patients:

#### POSTOPERATIVE MENSTRUAL HISTORY

DURATION OF MENSTRUATION	NO. OF CASES OBSERVED
10 years	14
9 years	16
8 years	5
7 years	8
5 years	6
4 years	8
2 years	3
Total	60

Discreet and tactful questioning regarding libido following sterilization warrants the statement that it is unchanged in 25 per cent and decidedly increased in 75 per cent of these cases. The increased libido must be ascribed to the removal of fear of pregnancy. Patients report a definite improvement in sex life following sterilization.

As previously stated, no actual proof of the possibility of restoration of the continuity of the tubes can be offered. Should occasion arise, reconstruction ought to be possible. The invaginated portion of the uterine stumps could be resected, the distal ends removed from their artificial uterine canal and an end-to-end anastomosis obtained with very fine interrupted catgut sutures. This could be done either vaginally or abdominally.

There should be, and, so far, has been no mortality from the tubal reimplantation which has been used, as occasion demanded, for some twenty-two years. Analysis of the sixty follow-up cases has been extremely gratifying:

Mortality	None
Morbidity	5%
Omental adhesions	1
Dysmenorrhea	2
Psychic disturbances	None
Surgical amenorrhea	None
Libido	Unchanged 25%; Increased 75%

## SUMMARY

1. A simple, safe and, so far, uniformly successful method of tubal sterilization is reviewed, sixty cases being analyzed as to morbidity and end-results.

2. The operation should never be undertaken in the presence of any acute abdominopelvic infection, but subacute or chronic pathologic conditions can be removed at the same time without increasing the incidence of mortality or morbidity.

3. The principle of the operation is based on the belief that preservation of tubal excretion prevents the possible formation of an aseptic hydrosalpinx.

4. Ovarian function is not disturbed.

5. On theoretical grounds the operation can be used as a temporary means of sterilization.

## REFERENCES

- (1) Tarnowsky, G. de: Tubal Reimplantation, J. A. M. A. 60: 893, 1913. (2) Bush, L. E.: Am. J. Surg. 24: 3, 1934. (3) Aldridge, A. H.: AM. J. OBST. & GYNEC. 27: 741, 1934. (4) Slemons, J. M.: AM. J. OBST. & GYNEC. 27: 775, 1934. (5) Scheffzek, F. A.: Zentralbl. f. Gynäk. 58: 2786, 1934. (6) Hyams, M. N.: AM. J. OBST. & GYNEC. 28: 96, 1934. (7) Culbertson, C.: Surgery of the Female Pelvis, New York, 1923, D. Appleton-Century Co., p. 319. (8) Naujocks, H.: Zentralbl. f. Gynäk. 55: 81, 1931. (9) Rubovits, W. H., and Kobak, A. J.: AM. J. OBST. & GYNEC. 27: 12, 1934. (10) Fuchs, H., and Lork, E. C.: Montaschr. Geburtsh. u. Gynäk. 88: 199, 1931. (11) Walz, W.: Zentralbl. f. Gynäk. 56: 2007, 1932. (12) Madlener, M. M.: Zentralbl. f. Gynäk. 56: 2731, 1932. (13) Malcrieff: Gynec. et obst. 25: 217, 1932. (14) Granella, C.: Zentralbl. f. Gynäk. 57: 938, 1933. (15) Kulenkramppf, D.: Deutsche med. Wchnschr. 59: 1294, 1933. (16) Chamarro, J. A.: Semana méd. 2: 449, 1933. (17) Zocchi, S.: Boll. d. soc. piemontese di ost. & ginee. 1: 198, 1933. (18) Saenger: Arch. f. Gynäk. 156: 157, 1933. (19) Rosenberg, M.: AM. J. OBST. & GYNEC. 24: 154, 1932. (20) Zomakion, A.: Zentralbl. f. Gynäk. 49: 2404, 1925. (21) Vignes, H., and Barron, F.: Bull. Soc. d'obst. et de gynec. 4: 225, 1931. (22) Baskin, M. J.: AM. J. OBST. & GYNEC. 24: 892, 1932. (23) Curtis, A. H.: Obst. & Gynec. 111: 224, 1933. (24) Turenne, A.: Surg. Gynec. Obst. 29: 577, 1919. (25) Jackson, G. B.: J. A. M. A. 99: 2026, 1932.

30 NORTH MICHIGAN AVENUE

---

Ghosh, Sudhangsu Kumar: An Unusual Case of Traumatic Haemorrhage From the Vagina, Calcutta M. J. 29: 173, 1934.

The author reports a case of rupture of posterior wall and fornix of vagina during intercourse, in a multipara, aged twenty-six, causing profuse hemorrhage. Patient was confined six months previously and had had puerperal fever for several weeks.

It was the first coitus after delivery, followed by free blood discharge. Examination showed a lacerated wound in posterior vaginal wall longitudinally from 1 inch above introitus to posterior fornix,  $2\frac{1}{2}$  inches by 1 inch and muscle deep. No scar tissue was seen in vagina. Sutures had to be passed through fascial layers.

Fatal coitus injuries are on record. After prolonged illness the soft attenuated vagina yields easily to small pressure. In this multipara, the vaginal tissue was possibly abnormally soft.

F. L. ADAIR AND S. A. PEARL.

## HEMATOMETRA\*

JOHN A. MCGLINN, M.D., F.A.C.S., AND  
W. BENSON HARER, M.D., F.A.C.S., PHILADELPHIA, PA.  
(From the Departments of Gynecology of the St. Agnes Hospital and  
Fitzgerald Mercy Hospital)

**H**EMATOMETRA is a condition that has received but scant attention in recent medical literature. Even in such a comprehensive work on obstetrics and gynecology as the new Curtis textbook, we find it referred to only in connection with congenital malformations of the genital tract and then in a very incomplete form. Reference on this subject in recent years has been limited practically to simple case reports, owing probably to the relative rarity of the condition. However, hematometra is undoubtedly becoming more frequent and this fact, together with certain points of unusual interest in two of our recent cases, prompts us to present this report.

No definite statement can be made concerning the incidence of hematometra. The condition is so rare that many gynecologists of broad experience have never encountered a case. In certain countries, however, the condition is becoming more common. Thus, in Russia in eighteen months prior to January, 1927, twenty cases of hematometra occurred in one series of 1,500 cases of induced abortion as a result of atresia of the cervix due to improper curettage.

Etiologically, hematometra is always the result of an occlusion of the genital tract at some point external to the uterine cavity. This occlusion may be either congenital or acquired and may be either a complete occlusion of the genital tract or, more rarely, may at first be only a partial occlusion. The congenital cases are due to malformations of the genital organs, such as imperforate hymen, absence of vagina, uterus duplex unicollis with no cervical opening, double vagina in which one canal is blind, etc. Such cases at times constitute most difficult gynecologic problems but fortunately are quite rare. The more commonly encountered cases are those due to an acquired atresia of the lower genital tract. In such cases the occlusion frequently is the result of overzealous curettage of the uterus and especially of the cervical canal, improper cauterization of the cervix from the use of too heavy a cautery tip, or the application of caustics to the cervix. The increasingly frequent application of radium to the cervix and uterine cavity in the treatment of cervical or fundal carcinoma and of menorrhagia or metrorrhagia due to other causes is

---

\*Read at meeting of the Obstetrical Society of Philadelphia May 2, 1935.

resulting in an ever increasing incidence of cervical atresia. This usually follows the use of improperly screened radium by relatively inexperienced operators. Another etiologic factor in the production of an acquired hematometra is adhesions of the cervical canal or vagina resulting from infections of the birth canal. One of our cases, in which the vaginal atresia was the result of a gonocoeal infection, well illustrates this point, but is unusual in that such oclusions are quite uncommon as a sequel of gonorrhea. Still another etiologic factor that should be stressed today is atresia of the vagina resulting from improper use of the Elliott treatment of pelvic inflammatory conditions. Although of undoubted value, this treatment is not without danger; especially when, as is frequently the case, its application is entrusted to a nurse or office attendant. Recently, a number of cases of severe burns of the vagina, several with complete atresia, have been reported following such treatments.

The signs and symptoms of hematometra depend somewhat upon the site of the genital occlusion and whether this occlusion is partial or complete. If partial, the patient complains of severe dysmenorrhea and greatly prolonged menses with the passage of black, tarry material. This recurs for a variable number of times, generally with progressively increasing severity until eventually the occlusion of the genital tract becomes complete, after which the lower abdominal pains, backache, headache, general malaise, etc., continue to recur but with no accompanying vaginal discharge. If the site of occlusion is in the lower part of the vagina, the pain becomes marked in this region and swelling of the vulva with bulging of the perineum much like that seen in labor appears. Later on, prominence of the lower abdomen develops and on palpation a rounded mass closely resembling a pregnant uterus may be felt. If the condition is allowed to proceed still further, the tubes then become distended and may be felt as large, tender, fluctuating, sausage-shaped masses in the pelvis or lower abdomen. If the fimbriated end of the tube remains patulous, these masses slowly decrease in size in the intermenstrual period and may even return practically to normal size. Such a discharge of menstrual fluid into the abdominal cavity gives rise to all the signs and symptoms of a chemical type of peritonitis and eventually results in the production of an endometriosis.

These signs and symptoms first appear at puberty in all congenital and in some acquired cases of hematometra. In such cases, when the occlusion of the genital tract is complete there is a history of complete amenorrhea together with the signs and symptoms just described. In those acquired cases, occurring later in life, there is a history of normal menstruation up to the time of occurrence of the condition or opera-

tion which produced the genital atresia, after which there is amenorrhea and the development of the above described symptoms.

The pathology of hematometra is quite interesting. If the site of occlusion is near the vulva, the vagina, because of the elasticity of the walls, first balloons out with the menstrual fluid, resulting in the development of hematocolpos. The uterine muscle at first becomes greatly hypertrophied as a result of the efforts made to expel the menstrual blood. Accompanying this muscular hypertrophy we have marked thickening of the endometrium. Eventually the accumulation of blood in the vagina reaches the stage of maximum distensibility of the vaginal tissues and then the uterus begins to distend and hematometra results. The increasing intrauterine pressure causes atrophy of both the endometrium and uterine muscle. This endometrial atrophy tends to somewhat lessen the quantity of menstrual blood produced during each period and so somewhat retards the further development of the condition. However, in time, the menstrual fluid is squeezed out into the fallopian tubes, distending them and then spilling out into the peritoneal cavity. The abdominal spill sets up a chemical type of peritonitis with the usual result of formation of dense adhesions particularly in the culdesac and to the posterior uterine wall. Since viable endometrial cells are frequently present in the menstrual discharge, these cells may lodge on the ovary due to its close proximity to the end of the tube and so give rise to ovarian endometriosis. Finally, as a result of the prolonged irritation by the menstrual blood and the formation of adhesions, the tubes become sealed off at the abdominal end. From this time on there is only continued distention of all affected parts and marked increase in symptoms until treatment is given or rupture occurs.

Time and space do not permit a full discussion of the differential diagnosis of hematometra. Among the commoner conditions which hematometra may simulate may be mentioned the delayed onset of the menses at puberty, pregnancy with threatened abortion, acute appendicitis, relaxation of the sacro-iliac joints, pelvic inflammatory disease, peritonitis, and endometriosis. A careful history and thorough physical examination should suffice to differentiate these conditions in most cases.

The treatment of hematometra depends upon the duration and the cause of the condition. In cases occurring at puberty where the condition is recognized before hematosalpinx has developed, simple vaginal drainage secured by incision of the occluding membrane or lysis of adhesions, is all that is required. The surgical correction of any congenital abnormality of the genital tract is, of course, indicated. In neglected cases, vaginal drainage is contraindicated because of the danger of subsequent peritonitis from ascending infection of the genital tract. All neglected cases and most acquired cases of hemato-

metra occurring later in life are best treated by laparotomy and removal of all pathologic tissue. Occasionally, conservative treatment by vaginal drainage may be employed in acquired cases occurring later in life.

#### CASE REPORTS

CASE 1.—Mrs. M. B., aged forty-five, para ii, last child nine years ago. Chief complaints: Backache and severe pain in lower abdomen. Patient was perfectly well until after the birth of her first child, twelve years ago, then began to suffer with profuse and prolonged menstrual periods. She was treated without much relief and finally was advised to become pregnant again in the hope that another pregnancy might clear up this condition. She followed this advice, but with the resumption of the menstrual function following the birth of her second child, the menorrhagia again returned. Six years ago radium was inserted in the uterus to control the uterine bleeding. Following this she had no vaginal bleeding at any time. She was then well until about two years ago when she began to suffer with severe pain in the back, in the lumbosacral region. This pain began abruptly and continued for five days, during which time she first consulted one of us (W. B. H.). Examination at that time failed to reveal any definite cause for the pain and the condition cleared up under symptomatic treatment. About three months later she suffered a similar attack, which again cleared up after about seven days. The patient was then not seen until about nine months later when she returned, complaining of pain in the back and severe cramplike pains in the lower abdomen. She stated at this time that the attack of pain had come on about two weeks previously and this time had lasted for about nine days. She further stated that she had been thoroughly studied in one of the large hospitals of Philadelphia for a period of six weeks and had been told that she had visceroptosis, a severe secondary anemia and a floating tumor the size of an orange in the region of the left fallopian tube. Examination at the time of this visit revealed no evidence of such a tumor even though the patient was examined in both the reclining and erect positions. Following this visit the patient was again lost sight of until March, 1934, when I was called to see her at her home. At this time she was suffering with very severe pain in the lower abdomen which had started the previous day. Examination at this time revealed rigidity and marked tenderness over the entire lower abdomen. Before a vaginal examination could be done, the patient then volunteered the information that in the interval since I had last seen her she had had a similar attack during the acute stage of which she had been examined by another gynecologist who told her that she had fibroids and strongly urged that she undergo a course of x-ray treatments for this condition. Vaginal examination at this time revealed a symmetrically enlarged, hard, tender uterus and a soft cystic mass about the size of a small grapefruit in the left adnexal region. I told the patient that I agreed with the diagnosis of fibroids but that she also had an ovarian cyst and that therefore she should be operated upon rather than treated with x-rays. The next day she again called me and agreed to go to the hospital. After carrying out the usual preliminary work, the patient was given 90 mg. of avertin per kilo of body weight. An attempt was made to do a preliminary dilatation and curettage but no opening could be found in the cervix. The true diagnosis was then apparent and laparotomy was immediately performed. The uterus was symmetrically enlarged about the size of a four months' pregnancy. The right tube and ovary were bound down into the culdesac with dense adhesions. This tube was greatly distended and sausage-shaped. The left tube was greatly enlarged, black in color and black fatty blood was oozing from the fimbriated end of the tube. The left ovary contained a large chocolate cyst. The entire pelvic organs were bound down to the sigmoid, small intestines and omentum by dense adhesions. After free-

## A CONSIDERATION OF THE PHENOMENON OF OVULATION AND ITS RELATION TO THE SEX CYCLE\*

IRVING F. STEIN, B.S., M.D., F.A.C.S., CHICAGO, ILL.

*(From Northwestern University Medical School and Michael Reese Hospital)*

THE phenomenon of ovulation is fundamental to the reproductive process, but our knowledge concerning the exact time of occurrence of this phenomenon in the human being, the mechanism thereof, and its relation to the associated changes in the sex cycle is still far from complete. Our understanding of the endocrine stimulation of ovulation is just beginning to dawn, and the relationship between ovulation, corpus luteum formation, and menstruation is being acknowledged. The analogy of the sex cycle in the human being to that of lower mammals inclines one to accept certain facts revealed by animal experimentation and to apply them directly, but one outstanding observation tends to cast doubt upon such analogies, namely, that the function of menstruation is to be observed in the primates alone. The great variation which exists in the gestation periods in mammals, from twelve or thirteen days in the opossum to nearly two years in the elephant, suggests that there may also be great discrepancies in the fecundity of ova and spermatozoa as well as in the conditions for mating. In lower animals, mating is usually restricted to a few hours or days before ovulation, while in primates there is no set rule. While in all mammals one observes certain similarities in pattern, there are also differences both in the structure and the function of many organs. The human organism stands out as being unique, and as Beaumarchais so aptly said, "Drinking without being thirsty, and making love at all seasons distinguishes man from beasts." In some of the smaller mammals, copulation stimulates ovulation. This is true according to Allen, in the cat, rabbit, and ferret; in others, spontaneous ovulation is the rule. In primates, ovulation is probably spontaneous, yet it is not definitely known whether in certain females the stimulation of coitus may not induce multiple ovulation and follicle rupture at variable times in the cycle. According to the most recent opinion (Ball and Hartman), ovulation is not ascertainable with accuracy in women at the present time. The pituitary extract test of Knaus, though a valuable one for experimentation, is not applicable clinically. Frank's hormone test, though an excellent one, must be simplified for practical usage.

With a view to stimulating further thought upon this fundamental question, I desire to present what data I have been able to assemble in

\*Presidential Address before the meeting of the Chicago Gynecological Society, June 7, 1935.

as simple a form as possible. I have very little that is original to offer; merely the kernels which I have gathered from the sources which were available to me.

#### EVIDENCE OF OVULATION TIME IN WOMEN

L. Fraenkel was the first to show that ovulation precedes menstruation. From evidence obtained by the examination of the ovaries at operation, he concluded that ovulation occurred on the eighteenth day of the cycle. Schroeder from a study of operative material also placed ovulation at the fourteenth to sixteenth day in regular four-week cycles, and Meyer and Ruge stated it to be on the eighth day or during menstruation itself, and later (Ruge, 1919) concluded that ovulation occurred on the eighth to the fourteenth day in the cycle.

Ogino placed ovulation on the twelfth to sixteenth day before the onset of the next menstruation (after examining 118 women at laparotomy), and Knaus concluded from his work that in women with normal reproductive physiology, ovulation always takes place on the fifteenth day before the onset of menstruation.

Asdell, after a study of 568 cases in which operative and autopsy material was used, stated that the period of ovulation is variable in the menstrual cycle, occurring most frequently between the eighth and seventeenth days.

Additional evidence of the time of ovulation is presented by Allen, Pratt, Newell and Bland by obtaining 5 young human ova at operation. Of their 40 observed patients, 26 operations were performed between the twelfth and sixteenth days of the cycle. The ova obtained by tubal washing were found, 1 on the fourteenth, 3 on the fifteenth, and 1 on the sixteenth days. They concluded from the condition of the ova when found that ovulation occurred in these women between the twelfth and fourteenth days after the first appearance of the previous menses. Lewis recovered one ovum on the eighteenth day after a previous cycle of thirty-five days and Hyrtl found one in the interstitial portion of the tube on the fourth day (DeLee). In this connection, Swezy comments that when the number of tubal eggs found is compared with the number of cases examined during the middle of the cycle, with not only *no evidence* of ovulation, but with the uterus and ovary in the anestrus or resting phase, it is strong evidence that this test is inadequate. He considers the *amount of proliferation* of the endometrium to be the criterion upon which to judge ovulation time.

From data obtained by measuring the size of graafian follicles, Allen and Papanicolaou concluded that ovulation might occur anywhere from the second to the twenty-eighth day of the cycle. From another angle, Teacher tabulated time of fertilization and embedding of the ovum estimated from the study of early ova as reported by various authors. As may be seen (Table I), fertilization was estimated to have occurred throughout most of the cycle, from the sixth to the twenty-eighth day, and embedding from the thirteenth to the twenty-eighth day of the current cycle and through the fourth day of the succeeding one. In addition, Triepel estimated the ovulation time from observations upon early embryos and found it to be the eighteenth or nineteenth day of the cycle; Grosser on the second to the twenty-fourth day, and Volkmann, fourth to the twenty-fifth day (Table II).

Frank studied the quantitative anterior pituitary-like hormone and blood estrin throughout the cycle along with the urinary estrin excretion. He found an acute rise in anterior pituitary up to the time of follicle ripening, followed by a gradual fall to zero just before menstruation. At the same time, the blood estrin rose



acutely after ovulation to reach its height at the onset of menstruation, followed by a rapid drop during the period. Meanwhile the urinary estrin increased irregularly, reaching a peak about three days before menstruation.

TABLE I. ESTIMATED TIME OF FERTILIZATION AND EMBEDDING FROM STUDY OF EARLY OVA (TEACHER)

FERTILIZATION	DAY OF CYCLE	EMBEDDING
Merttens	6	
Rossi Doria	7	
Bencke	8	
Eternod	13	Merttens
	14	Rossi Doria
	15	Bencke
Peters	16	
Jung	17	
Von Spee (Glavecke)	19	
Von Spee (Von Herff)	21	Eternod
Frassi	23	Peters
Teacher, Bryce, and Reichert	24	Jung
Leopold	25	
	26	Von Spee (Glavecke)
	28	Von Spee (Von Herff)
	After menses	
	2	Frassi
	3	Teacher, Bryce, and Reichert
	4	Leopold

TABLE II. ESTIMATED TIME OF OVULATION FROM THE STUDY OF EARLY EMBRYOS

Triepel	18th or 19th day
Grosser	2nd to 24th day
Volkman	4th to 25th day

Knaus claims to have determined the exact time of ovulation by ascertaining the extent to which the human uterus loses its sensitiveness to posterior pituitary extract, in the presence of the corpus luteum hormone. This test requires the placing of a balloon into the uterus and of making manometric tracings on a kymograph. In women with a twenty-eight-day cycle, the uterus reacts with spontaneous rhythmic contractions in the first fourteen days and responds to pituitary stimulation. The capacity of the uterine cavity is 3 or 4 c.c. in the first two weeks, but on the sixteenth day increases to 8 to 10 c.c., is flaccid, and shows almost no spontaneous contractions. Now, it no longer responds to pituitary stimulation until the twenty-ninth day or twenty-four hours before menstruation, when it resumes the activity of the first half of the cycle.

Knaus believes that this test may be used as an accurate gauge of ovulation time, corpus luteum secretion causing abolition of spontaneous uterine contractions and rendering the uterus unresponsive to pituitary extract.

Particular significance is placed upon evidence obtained from the study of the reproductive cycle in the monkey, which, in some respects at least, is comparable to that in the human being. Thus, Ivy states, "In monkey and man it is generally agreed, and I consider it proved, that 'spontaneous' ovulation occurs about the middle of the twenty-seven- or twenty-eight-day cycle." On the other hand, Allen says that while in the monkey ovulation occurs on the thirteenth or fourteenth day, and in some cases as early as the tenth or eleventh day, that the ovulation time in primates may vary beyond these limits in irregular cycles, and that mating stimuli might possibly induce ovulation at other times. Fertile coitus in the monkey ranged from the ninth to the eighteenth days in the sixty cases observed by Hartman.

The discovery of a reliable and practical clinical test for ovulation appears to be near at hand, but is not as yet within our grasp. There is much that requires elucidation.

#### LIFE OF THE OVUM

The exact endocrine "hook-up" responsible for follicle development and ovulation is not as yet definitely known, but is at present assumed to be a reciprocal relationship between the hormones from the ovary and the anterior lobe of the pituitary gland. In the rabbit the actual process of ovulation has been observed, the rupture of the follicle occurring slowly, accompanied by a flow of thick, viscid, blood-tinged fluid. In the human being, the follicular fluid is thin and under considerable pressure, so that the actual mechanism of rupture may not occur in just the same manner, but may be more precipitous. Midmonth pain, when it occurs, but by no means the rule, is probably caused by rupture of the mature graafian follicle. After rupture, the ovum, free in the peritoneal cavity, finds its way into the fimbriated end of the fallopian tube. The mechanism of transit from the ovary to the tube, whether by chemotaxis, by suction set up by the ciliary wave, or enzyme action, is not understood as yet. More definite knowledge is at hand, however, concerning life of the mammalian ovum (Table III).

TABLE III. LIFE OF THE OVUM (IVY)

	HOURS	DAYS	EVIDENCE
Rabbit	4-5		Certain
Opossum	24		Certain
Mouse	24		Certain
Sow	24		Certain
Dog		5-6	Not certain
Human	48		Not certain

According to Knaus, the unfertilized human ovum has a very short life, possibly less than twelve hours. Degenerative changes, he states, set in within a few hours after extrusion and a laminated layer of follicular cells, the corona radiata, surrounds the ovum. These follicular cells are soon shed and an albuminous sheath which is supposedly derived from the tubal epithelium forms about the ovum. This sheath is impenetrable to spermatozoa, thus limiting the period of fertility to a few hours after extrusion from the follicle. This view presupposes that one and only one ovum is available for fertilization during each cycle. On the other hand, in the laboratory of Dr. Otto Saphir, I have observed sections of the human ovary with the three maturing follicles near the surface of the cortex, each containing an ovum which might possibly be extruded on different days of the same cycle (Fig. 1). Stockard and Evans have both suggested the probability of extraovulatory ovulation.

It is furthermore generally held that the presence of the corpus luteum inhibits further ovulation, and that a single corpus luteum is to be

found in the ovary during the last two weeks of each cycle. Exceptionally, I have seen two recent corpora lutea at slightly different stages

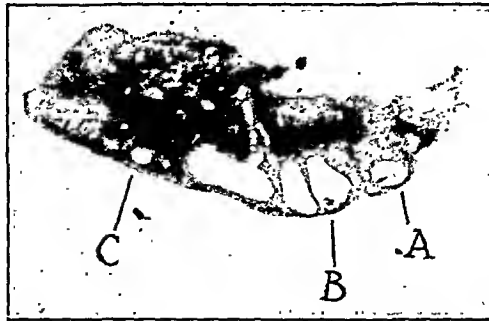


Fig. 1.—Section of human ovary with three maturing graafian follicles.



Fig. 2.—Left, high power of A and B shown in Fig. 1. Right, higher power of A, showing ovum.

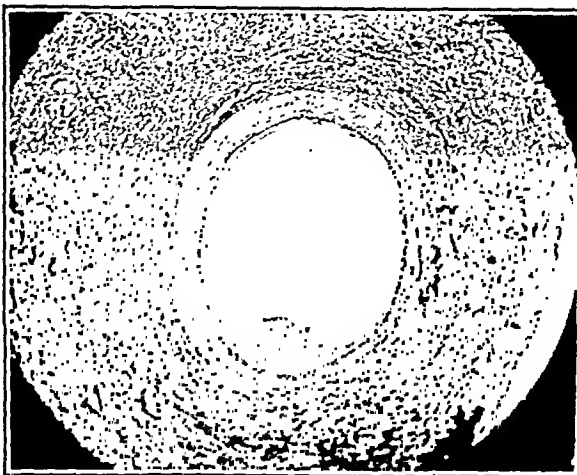


Fig. 3.—High power of C shown in Fig. 1.

of development in the section of an ovary which indicated the maturation of two ova in the current cycle. These observations tend to throw

considerable doubt upon the sterility-fertility rhythm theory as propounded by Knaus and Ogino, dependent as it is upon a single ovum at a fixed time in the cycle.

#### LIFE AND FECUNDITY OF SPERMATOOZA

More than twenty years ago, Hoehne and Behne stated that human spermatozoa cannot remain fertile in the fallopian tubes longer than three days. The sperms probably reach the fimbriated end of the tube and the peritoneal cavity within a few hours after coitus, but according to Dührssen and Nürnberger may live in the infundibulum of the tube for at least three weeks. Many authors believe, however, that the fertilizing power of the sperms is short, probably not more than three days. Knaus says it is less than two days, and this holds for the spermatozoa of all mammals with scrotal testes; that the intraabdominal temperature plus the alkaline secretion of the fallopian tubes tend to limit their

TABLE IV. LIFE OF SPERMATOOZA (KNAUS)

	HOURS
Rabbit	30-48
Rat	12-16
Guinea pig	41
Pig	41½
Horse	48
Bat	Several months (all winter)
Human	48 (or less)

fecundity. Spermatozoa kept at body temperature in vitro remain fertile for about sixteen hours, and at the freezing point for about seventy-two hours. They remain fertile longer at room temperature than in the incubator, and longer in the vagina of a dead animal than one alive. Knaus believes that the life of the human spermatozoa in the uterus and tubes is considerably shorter than in animals. He says that the overabundance of sperms which are provided at coitus is an absolute necessity for fertilization, for only a few can survive the powerful defense works of the mucosa of the female generative tract. He also states that this defense is less powerful at the time of ovulation.

It appears to me to be unreasonable to ascribe to the generative organs a quality of defense, placing great obstacles in the way of the male germ cells when the prime function of those organs is reproduction. Does nature intend that reproduction be made intricate and difficult, or is the mechanism set up for safety and protection of the male and female egg?

#### CONCEPTION LIMITATIONS

Knaus and Ogino independently have determined that ovulation occurs regularly on the fifteenth or sixteenth day, before the appearance of the succeeding menstruation. They are agreed that the fertile period is

limited to approximately three days before and two days following ovulation. They have accumulated considerable clinical data to substantiate their claims. Furthermore, Miller, following the fertility-sterility rhythm of Knaus and Ogino, reported on 126 couples who held intercourse 1,429 times in the "sterile" portion of the month without the occurrence of a single conception, and 49 instances of coitus between the twelfth and nineteenth days of the cycle resulting in conception.

On the other hand, Dickinson assembled a mass of evidence from various sources from which he adduced that: (1) Conception can occur at any part of the month. (2) There is a very marked difference between favorable and unfavorable periods (72 per cent in the first two weeks, about 7 per cent in the premenstrual or "sterile" week, and 13 per cent during menstruation). He also showed that the days of the month of maximum sex desire and maximum well-being occurred simultaneously at the time of *minimum* chance for conception, namely, in the premenstrual week. This would indicate that woman by nature is led to cohabit most frequently when chances for pregnancy were low, or, according to Ogino and Knaus, *were nil*. By comparison with the monkey, this is indeed inconsistent, for most recent studies indicate (Ball and Hartman) that sex desire in the monkey reaches its height just *prior to ovulation*, and that the premenstrual rise which occurs in women is entirely absent.

One can hardly ignore the accumulated data of conceptions occurring in women with twenty-eight-day cycles and resulting from single acts of coitus; 1,342 cases were assembled by Dickinson in which no days of the month were exempt; most conceptions occurred after coitus on the sixth, seventh, and eighth days, 72 per cent in the first two weeks, about 13 per cent during the menses, and from 7 to 10 per cent in the fourth week of the cycle. Fraenkel, on a recent visit to this country, expressed an opinion which entirely coincides with that published by Dickinson. His personal series of almost 200 cases of isolated coitus showed about the same proportions of conceptions distributed similarly in the cycle as those quoted above, and he concluded that there is no regular safe period for women. Furthermore, he emphasized that a minimum of women menstruate regularly every twenty-eight days.

#### COMMENT

There is a growing literature encompassing valuable data concerning the phenomenon of ovulation and its relation to the sex cycle. As yet, we have no practical clinical test for ovulation nor do we entirely comprehend the detailed mechanism of follicle rupture and tubal entrance. As a matter of fact, we must admit that, although we have amassed much information, we possess very few facts. We are intrigued by the theory of a fertility-sterility rhythm in women and we look forward eagerly to the next decade of carefully collected clinical data concerning its application. If nature has provided a definite safe period before the

twelfth day and after the nineteenth day of the regular twenty-eight-day cycle, it is indeed contrary to the principle of perpetuation of the species to place the period of maximum sex-desire and euphoria exactly in the sterile phases of the sex cycle. There is a discrepancy somewhere, and it becomes the task of the clinician and physiologist to jointly weld the chain of facts.

In closing, I would urge physicians to collect accurate data concerning the exact menstrual cycle in their patients, and note such facts as time of intercourse, midmonth pain, and sex desire. The calendar method appears at present to be adequate for literate women. If such data would be assembled, then in a few years we would, in all likelihood, be enabled to answer some of the perplexing questions concerning human reproduction.

## REFERENCES

- (1) *Allen, E.*: Sex and Internal Secretions, Baltimore, 1932, Williams & Wilkins Company. (2) *Allen, Pratt, Newell, and Bland*: *Am. J. Anat.* 46: 1, 1930. (3) *Ball and Hartman*: *AM. J. OBST. & GYNEC.* 29: 117, 1935. (4) *Corner, G. N.*: *Carn. Inst. Cont. Embryol.* 13: 117, 1921; 15: 73, 1923. (5) *Davis, K. B.*: *Factors in the Sex Life of 2,200 Women*, New York, 1929, Harper & Brothers. (6) *DeLee, J. B.*: *Principles and Practice of Obstetrics*, ed. 5, Philadelphia, 1929, W. B. Saunders Co. (7) *Dickinson, R. L.*: *AM. J. OBST. & GYNEC.* 14: 718, 1927. (8) *Evans, E., and Swezy, O.*: *Am. J. Physiol.* 96: 628, 1931. (9) *Frank, R. T.*: *J. A. M. A.* 103: 394, 1934. (10) *Hartman, C.*: *Science*, p. 226, 1931. (11) *Ivy, A. C.*: *Notes on Ovulation*. (12) *Knaus, H.*: *Periodic Fertility and Sterility in Woman*, Vienna, 1934. (13) *Norak, E.*: *Menstruation and Its Disorders*, Monographs, New York, 1931, D. Appleton-Century Co. (14) *Ogino, K.*: *Conception Period of Women*, Harrisburg, Pa., 1934. (15) *Saphir, Otto*: Personal communication. (16) *Swezy, O.*: *AM. J. OBST. & GYNEC.* 29: 246, 1935.

310 SOUTH MICHIGAN AVENUE

---

Gasquet, P.: *The Treatment of Pruritus Vulvae by Infiltration With Radon in the Pruritic Area*, *Rev. franç. de gynéc. et d'obst.* 29: 1079, 1934.

In many cases of pruritus vulvae, local treatment is of no avail. The subcutaneous injection of novocaine solution has only a temporary effect. Radiotherapy is followed by certain accidents. Resection of the presacral nerve requires an operation. Gasquet applied radon or the emanation of radium externally but the results were not entirely satisfactory. He, therefore, resorted to the subcutaneous injection of radon into the area of pruritus. He gives daily injections and sometimes only three a week of between 400 and 800 millimicrocuries of radon. The injection is never painful. The relief sometimes manifests itself after the first injection but more often after the third. The author has never had to give more than 15 injections. The action of the radon is on the terminal nerve endings from where, because of its affinity for nerve tissue, the radon ascends as high as the nerve trunks, thereby producing a sedative action upon the territory innervated by these nerves. The treatment is entirely innocuous as proved by the total disintegration of the radon within about a month after it is administered. This holds true regardless of the dose injected.

J. P. GREENHILL.

# A CLINICAL TEST OF THE NEWLY RECOGNIZED OXYTOCIC PRINCIPLE OF ERGOT AND A NEW METHOD OF ADMINISTRATION

VERNON L. TUCK, M.D., SHERMAN, TEXAS

CONSIDERABLE has been said in the recent medical literature with reference to a previously unrecognized oxytocic principle of ergot and the manner in which it proves its superiority over the older preparations in initiating uterine contractions. At the time of this writing it seems well established that a pure crystalline substance has been isolated by Thompson,<sup>1</sup> and Dudley and Moir<sup>2</sup> from ergot, of definitely alkaloidal nature, which gives rather startlingly splendid results when used in various ways as an oxytocic. The results would indicate that the two groups working separately have been successful in isolating the same alkaloid. Another article<sup>3</sup> calls attention to the fact that the Baltimore worker no doubt was the first to appreciate the true alkaloidal character of the product. Thompson has given the name ergostetrine and the English group have utilized the term ergometrine for their respective alkaloids. At about the same time, in this country, a Chicago group, Davis, Adair et al.<sup>4</sup> reported the isolation of a non-alkaloidal fraction of ergot which they have produced in crystalline form, that seems to possess the same degree of activity as attributed to the acknowledged alkaloidal crystals of the other workers. Dudley and Moir<sup>3</sup> object for obvious reasons to the name ergotocin given to this third product since it was applied originally to a more crude extract rather than to the purified crystalline form. Regardless of the name of the ergot derivative, however, and the priority of claim, all three are apparently superior to any other ergot preparation previously used. None of these workers attempted a method of administration which has proved in this clinical series more adequate than any other in quickness of action, ease of administration and consistency of results, namely, by rectum. However, Jones and Barlow<sup>5</sup> believe that the older ergot preparations give a more satisfactory result by this route.

The method of study in this series obviously differs from the procedure followed by the other investigators, since the object was to give the alkaloid a thorough clinical trial on the postpartum uterus and to form some ideas concerning its adequacy in controlling postpartum hemorrhage, maintaining good uterine tone during the early puerperium, the consistency of its actions by various routes of ad-

ministration, and the possibility of decreasing the incidence of morbidity by shortening the duration of the so-called normal period of lochia rubra and by hastening involution. These are in large the questions that interest the obstetric profession. Whereas the other investigators used the uterine bag and abdominal tambour methods of study, our method consisting of manual palpation of the fundus uteri and clinical observation may at a casual glance seem rather crude; however, it has proved quite satisfactory in the hands of the accoucheurs these many years. It can be readily understood that more elaborate methods cannot be followed routinely on the wards of a charity hospital where the obstetric turnover is so rapid.\*

The drug used in this series was furnished by Dr. M. R. Thompson, of the School of Pharmacy, University of Maryland, through the courtesy of John Wyeth and Brother. For hypodermic use the alkaloid ergostetrine was dissolved into a 20 per cent alcoholic solution standardized to contain 0.5 mg. ergostetrine per 1 c.c. which proved to be the optimum dosage for that mode of administration. However, the drug for oral and rectal use was a product containing 20 per cent alcohol (supplied as ergoklonin) standardized to contain 0.1 mg. ergostetrine per 1 c.c., and proved most satisfactory by both routes in one drachm dosages. All of the women participating in this study were in the third trimester of pregnancy and the drug was used immediately after the second or third stages of labor, as will be shown later. In initiating the study, a series of control cases was run in which our old hospital routine, consisting of U.S.P. ergot after the second stage of labor and one ampule of pituitary solution U.S.P. after the third stage, was carried out, but after running fifty alternate cases in this manner, the results were so promising with the newly recognized alkaloid that the control series was dropped. At no time in the remainder of the series was it necessary to supplement the new drug with any other oxytocic. Among the women delivered in the series there were: Primiparas 105, multiparas 227, episiotomies 61, forceps 23, versions 1, eclampsias 5, positive Kahn 12, breech 12, abruptio placentae 2, twins 2, and stillborn babies 15.

The selection of the most satisfactory mode of administration proved to be one of the most interesting phases of the study. The drug was given by mouth in the early cases and proved itself adequate. The one drachm dose, 0.4 mg. of ergostetrine, was diluted to 2 ounces with water, largely to assist in its passage rapidly through the pyloric sphincter of the stomach into the small bowel where it is rapidly absorbed. It is thought that absorption takes place more rapidly than

\*This series of cases was studied on the Obstetrical Wards of the Philadelphia General Hospital through the courtesy of the following chiefs: Drs. John A. McGinn, Harry A. Duncan, and Clifford B. Lull.



with the other ergot alkaloids due to the smaller size of the new alkaloid molecule. It seems almost unnecessary to add that a stomach distended with food tends to slow the passage of the drug into the small gut, and hence delays the onset of its oxytocic action. Irregardless of how the new oxytocic drug was given at the time of delivery, it was given orally in the one drachm dose diluted with two ounces of water three times daily on the first three postpartum days, as is routine on most obstetric services. The hypodermic route was used in some of the patients delivered under general anesthesia and offers no variation from the technic generally employed. Suffice it to say that to date no irritations or infections have resulted from its usage.

The rectal route, however, surpassed all expectations in offering a method of administering this drug. In retrospect, one wonders why a drug so commonly used in obstetrics over such a long period of time, as ergot, has not been given a thorough trial by the rectal route, especially when the anal dimple occupies such a central position in the field of a delivery. The ease of injection, speed of reaction and efficacy of uterine contractions require that this route be considered more in detail. A rubber catheter, size 18-21, has proved most satisfactory as a means of introducing the solution into the rectum. The catheter, lubricated with green soap or any other similar medium, is advanced three to four inches from the anus into the rectum or to any point inside the internal sphincter. While the tube is held in place the one drachm dose is diluted with two to three drachms of water and either forced through the catheter with a syringe or allowed to flow through by gravity after using a small funnel as a reservoir. Care should be taken to withdraw the tube slowly after injection, and it seems advantageous to have the tube clamped off with the fingers while pulling through the sphincter. In only one condition has it been necessary to insert the tube higher into the rectum and that is when the patient is so deeply anesthetized that there is complete relaxation of the anal sphincter. In this case, by introducing the catheter to about eight inches and allowing it to remain for one and one-half minutes after injection of the drug, followed by a slow withdrawal, all danger of leakage is obviated and in that time sufficient of the drug has been absorbed to give an entirely satisfactory oxytocic effect on the uterus. One other factor probably has been of definite advantage in avoiding a premature spill from the rectum. It has been given routinely only after expression of the placenta in order to avoid being expressed by massage of the fundus as is routine in some clinics. By observing these precautions, all danger of leakage is avoided and the mode of administration is certainly more simple and efficient than any we have previously tried.

The type of uterine contraction resulting from the use of the new alkaloid is characteristically different from that given by pituitary solution. Rather than giving a tonic spasm to the uterine musculature, it gives a clonic effect with very firm contractions lasting one and one-half to two minutes and followed by a mild degree of relaxation, but not sufficient to cause complete loss of tonus, as proved on kymographic tracings by a failure of the curve to return completely to the base line between contractions. Following the short interval of relative relaxation usually lasting about one minute, the cycle of contraction and relaxation is repeated over a period of several hours, showing a gradual decrease both in the tendency to return toward the base line during the periods between contractions and in the frequency of remissions or relaxations, thus leaving the uterus in a more or less contractile status. Irregardless of the method of administration, the uterine response has been consistently of this type and leaves no doubt in the mind of anyone palpating the fundus uteri as to the adequacy of contraction as well as to the absolute cessation of bleeding from the uterus.

At the present time, although the work has not been completed, 184 patients have been delivered, in whom only oral administration has been utilized. In the large majority of these the drug was given following the second stage of labor and at no time has there been a placenta retained in utero for longer than thirty minutes and in several instances the placenta was expressed into the vagina by the oxytocic alone. The onset of contractions was noted in these cases by the palpating fingers in three minutes as the shortest time and six minutes as the longest, the variation probably resulting from failure of passage of the drug into the small bowel in the more refractory ones. In studying the U.S.P. fluid extracts of various drug houses, the shortest time in which any of them worked orally was twelve minutes, and that with a variable response. This oral route was used chiefly in multiparous women who required only analgesia for delivery.

The hypodermic route was used in only twenty deliveries due to the splendid results from the rectal administration and our desire to give the latter route a thorough clinical trial. The contractions always resulted after hypodermic injection in from two to four and one-half minutes, being slightly more rapid in onset than after oral administration, but in no way giving a better result. Most of these patients were under general anesthesia and the administration whether after the second or third stage seems to be merely a matter of the obstetrician's preference.

At the present time 128 patients have been delivered with the new oxytocic being used only by rectum. The results have been astonishing and the procedure is being recommended, without reservation, to

the attention of the profession in order that it may get a wider clinical trial. In these cases there has been a contractile response on the part of the uterus in one to two and one-half minutes which differs in no particular from that resulting from the oral and hypodermic routes except in the speed with which it affects the uterus. It is of interest to note that a Gwathmey analgesia preceding the ergostetrine has in no instance delayed the latter's action. This is also true of a general anesthesia although the loss of sphincter control makes it necessary to use a little more care in giving the drug by rectum; but as pointed out previously, attention to two or three minor details will obviate the danger of expulsion and of contamination of the operative field. The rectal administration was routinely done after the third stage of labor for a definite reason as previously noted.

It can be positively stated that when the drug is given after the second stage of labor, there is a noticeable decrease in the amount of blood lost during the entire delivery. In addition it is important to note that no cases of even moderately severe postpartum hemorrhage have occurred; but at one time during the study a temporary lack of the newer drug necessitated the use of U.S.P. fluid extract of ergot and pituitary solution for about one week, and during this interval three moderately severe postpartum hemorrhages were encountered, two of them requiring uterine packing. With the new drug there was also a decrease in the oozing of blood from the uterus which is so frequently found for several hours after the patient leaves the delivery room. Ergostetrine administered by any route proved adequate to stop all uterine bleeding within a few moments whether given after the second or third stage of labor.

It is not the purpose of this paper to attempt to express definite opinions concerning the hastening of uterine involution by use of the new oxytocic. However, one is prone to think that there must be many advantages in its use since the lochia is almost free of a bloody tinge after three to four days when the alkaloid has been used in the early puerperium. DerBrueke<sup>6</sup> and many others are of the opinion that shortening the period of lochia rubra hastens involution. It is interesting to note the morbidity incidence in this series. Our morbidity standard is any elevation of temperature above 100° F. occurring twice in twenty-four hours, exclusive of the first twenty-four hours following delivery. The theoretical objection raised by many who have no practical experience with the rectal administration of the oxytocic is that there is imminent danger of its causing infection in the genital tract. This possible danger has not become apparent in this series, probably on account of the care with which the injection is given with our technic. Be that as it may, the morbidity (according to our standard) in 204 patients receiving the drug orally and

hypodermically was 14 per cent. On the other hand, in 128 patients receiving the drug rectally at delivery the morbidity was only 9 per cent. No maternal deaths occurred in this series. It would seem from these results that the rectal route when used properly offers no more danger of infecting the mother than the oral and hypodermic routes.

In summarizing, 332 women, advanced to the third trimester of pregnancy, were delivered using the newly recognized alkaloid as the only oxytocic in the second and third stages of labor. The results were uniformly satisfactory regardless of the mode of administration. No bad results were encountered and the action of the drug indicates that it is far superior to any of the older known oxytocic ingredients of ergot. The splendid response to rectal administration of the drug as evidenced by speed of reaction, consistency of results and ease of administration, makes it necessary to recommend its more widespread use in this manner by various obstetricians and to conclude that the rectal route is the optimum one so far tried.

Sincere thanks must be tendered the resident physicians and obstetrical nursing staff of the Philadelphia General Hospital, without whose able assistance this work would have been impossible.

#### REFERENCES

- (1) Thompson, M. R.: J. Am. Pharmaceutical Assn. 24: 185, 1935. (2) Dudley, H. W., and Moir, C.: Brit. M. J. p. 520, 1935. (3) Dudley, H. W., and Moir, C.: Science, p. 559, June 7, 1935. (4) Davis, M. E., Adair, F. L., Rogers, G., Kharasch, M. S., and Legault, R. R.: AM. J. OBST. & GYNEC. 29: 155, 1935. (5) Jones, J. L., and Barlow, O. W.: AM. J. OBST. & GYNEC. 29: 489, 1935. (6) DerBrucke, M. G.: AM. J. OBST. & GYNEC. 29: 272, 1935.

---

Oxley, Phillips and Young: Maternal Mortality in Rochdale—An Achievement in a Black Area, Brit. M. J. 1: 304, 1935.

Investigation of maternal mortality over a period of six years showed that obstetric factors, frequently preventable, were responsible for the high death rate in that area and not the existing economic ill conditions.

An interest in prophylaxis was stimulated by public propaganda. Antenatal care was increased. Improvement in the obstetric condition followed with a reduction in death rate from 8.9 in 1929 to 2.99 in 1932-34 per 1,000 live births registered.

The standard of maternity service directly affects the end-results. Admitting patients to a hospital early in labor and hospitalization during pregnancy and labor when abnormal conditions prevailed were responsible for better end-results.

By a deliberate effort this community achieved a reduction in its maternal death rate, by a method which may be adopted with success in other centers. This success is due to the mutual cooperation between the public health authority and all those engaged in the maternity services, as well as to the propaganda campaign inspired by the public health department throughout the borough.

The results were obtained by a change of spirit and method, without any alteration in the personnel or any substantial increase in public expenditure. A careful survey is recommended to each administrative area as routine practice.

F. L. ADAIR AND S. A. PEARL.

# PRIMARY CARCINOMA OF THE FALLOPIAN TUBE\*

## WITH REPORT OF A CASE

WALTER T. DANNREUTHER, M.D., NEW YORK, N. Y.

*(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)*

DAVID N. BARROWS<sup>1</sup> has published a comprehensive paper on primary carcinoma of the fallopian tube in which he reviewed the literature to date, discussed the etiology, symptomatology, and surgical treatment, and reported three cases from the Gynecological Service of Bellevue Hospital, admitted between the years 1911 and 1926. Calling attention to the frequency with which this neoplasm had been observed in the Gynecological Departments of the Johns Hopkins and Bellevue Hospitals, Barrows stated that "it begins to assume a frequency to force our consideration when we are dealing with adnexal conditions." Kahn and Norris<sup>2</sup> subsequently brought the literature further up to date, collecting 270 reported cases and adding four more of their own. Two of these occurred in young married women eighteen years of age, the youngest patients on record. These authors emphasize the apparent increase in the incidence of the disease during the past decade, but attribute this to a more highly "carcinoma-minded" profession and the greater number of excised specimens subjected to microscopic examination. A vivid recollection of Barrows' excellent presentation enabled me to make the correct diagnosis at operation in a recent case. Irregular bleeding from an apparently atrophic uterus and the presence of an obvious unilateral hematosalpinx, in a woman who had passed her menopause fifteen years previously, aroused the suspicion of tubal malignancy. The early diagnosis, miniature development of the lesion (Fig. 1), and complete extirpation of the pelvic organs in this patient encourage the hope that the prognosis is probably better than is usually the case.

### CASE REPORT

Mrs. L. B., aged fifty-seven, consulted me on Dec. 2, 1933, complaining of continuous vaginal bleeding for the previous five weeks. Her general health had always been good, and her only prior complaints had been constipation and leucorrhea. Menstruation began at fourteen, and had always been regular and painless. She had been delivered of three full-term babies after hard labors and had one spontaneous abortion. There was no history of pelvic inflammation. Menstruation stopped abruptly at the age of forty-two. Two years later she had one typical menstrual period, and never bled again until just before coming under observation.

\*Read before the New York Obstetrical Society, March 12, 1935.

The patient was well nourished but tremendously obese. Except for a blood pressure reading of 178/100, the general physical findings were normal. The portio of the cervix and vaginal fornix were fused in three places by bands of cicatricial tissue, but the cervix was not deeply lacerated or eroded. The uterine corpus was small, retroverted, and almost completely immobilized. The tubes on both sides were thickened and adherent, the one on the left side being distinctly larger. The ovaries could not be identified by palpation.

*Operation.*—Dec. 6, 1933. When the uterus was curetted, the endometrial surface was found to be atrophic. After opening the abdomen and freeing the pelvis of intestines, the findings on bimanual examination were verified. The left tube was larger than the right, densely adherent, and released with considerable difficulty. It was brownish red in color, clubbed and distended, and obviously contained old blood. A complete hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were done. Convalescence was uneventful until the eighth day, when there was



Fig. 1.—Low power photomicrograph of carcinoma originating in the left fallopian tube.

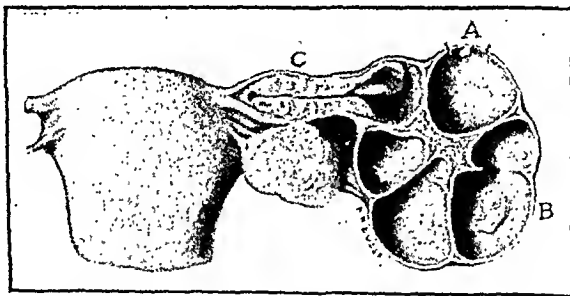


Fig. 2.—Uterus and sectioned left fallopian tube (right adnexa omitted from the drawing). A, point or origin of carcinoma; B, largest fragment broken off from the primary tumor and lying free in one of the cystlike compartments; C, hyperplastic plene and adherent blood clot at uterine end of the tube. (Semidiagrammatic.)

a dehiscence of the abdominal wound. This was resutured under infiltration anesthesia with through and through silkworm-gut sutures, after replacing three loops of intestine. Secondary union was perfect, and the wound is now well healed without evidence of hernia.

*Pathologic Report.*—Specimen was a uterus with tubes and ovaries. The uterus measured 35 by 20 by 30 mm. and the myometrium had an average thickness of 16 mm. The tube on the left side was approximately 80 mm. in length and had a proximal diameter of 5 mm. and a distal diameter of 20 mm. The fimbriated end was occluded and the entire tube was distorted and made tortuous by adhesions which bound it to the attached ovary. The ovary on this side measured 30 by 18 by 8 mm. and was markedly fibrotic. On section, the distal portion of the tube consisted of a number of thin-walled cysts containing brownish gray tissue fragments and hemorrhagic fluid (Fig. 2).

The other tube measured 40 mm. in length and had an average diameter of 6 mm. It was firm and cordlike, and the attached ovary measured 25 by 10 by 10 mm. and was equally firm. The fimbriated end of the tube was occluded by adhesions that bound it to the ovary. On section, the tube had a greatly thickened fibrous wall and the lumen was much narrowed. The ovary was buried in dense fibrous tissue.

Appendix was 40 mm. in length and 5 mm. in diameter. On section, the wall was moderately thickened. The lumen, a narrow slit, was filled with brownish material.

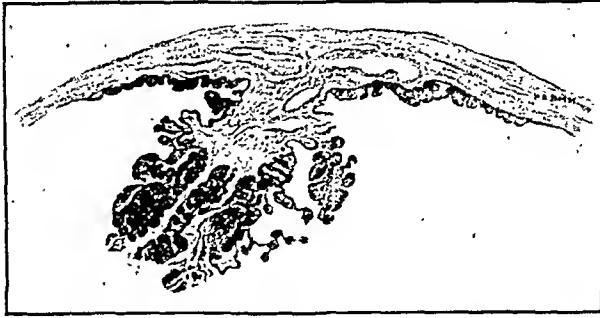


Fig. 3.—Drawing of the papillary excrescence, showing coarse convoluted papillae, formed by many layers of deeply stained cuboidal epithelium.

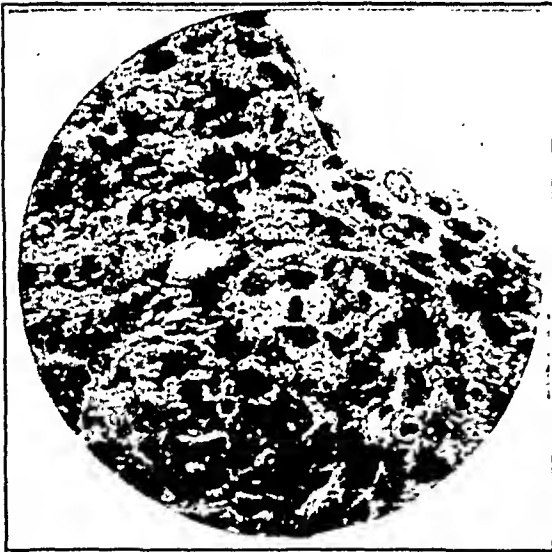


Fig. 4.

Fig. 4.—High power photomicrograph, showing anaplastic epithelium with mitotic figures.



Fig. 5.

Fig. 5.—Drawing of the largest detached fragment, showing structure similar to the atypical epithelium of the tumor attached to the tubal wall.

*Microscopic Examination.*—Sections of the uterus showed the endometrium lined by scattered epithelial cells, with an underlying layer suffused with blood and serum and infiltrated with lymphocytes and mononuclear cells. This layer was continuous with the stroma of the endometrium, which was scanty and also infiltrated and suffused with blood. The endometrial glands were scattered and rudimentary and were widely separated by the stroma, which was mildly infiltrated by lymphocytes in the deeper part. A few endometrial glands were dilated and were lined by one

or two layers of columnar cells which showed some exfoliation. The myometrium was more densely cellular than usual. The picture denoted curettage.

Sections of the dilated left tube showed a thin wall of fibrous tissue and a partial content of clotted blood, some of which clung to the inner wall. At one point there was papillary thickening with the formation of excrescences composed of deeply staining cells in which there were no lumina (Fig. 3). The epithelium was anaplastic, the cells showed very little cytoplasm, and mitotic figures were numerous (Fig. 4). This is evidently a highly malignant carcinoma, originating from the epithelium of the tube. The pieces of tissue floating in the hemorrhagic fluid exudate filling the dilated portion of the tube showed coarse convoluted papillae formed of many layers of deep-staining cuboidal epithelium. An occasional minute opening in the cell masses suggested tubule formation. The detached fragments showed a structure similar to the papillary excrescence arising from the dilated cystic tube and matched the atypical epithelium of the tumor attached to the tubal wall (Fig. 5). The proximal portion of the tube showed hyperplastic plicae covered by columnar epithelium. The plicae showed much increase in their fibrous stroma, which was mildly infiltrated by lymphocytes and mononuclear cells.

Sections of the other tube resembled the proximal portion of the first tube.

Sections of the left ovary showed corpora albicantia and numerous sclerosed blood vessels, with marked edema and congestion throughout. The tissues of the mesosalpinx in the adherent tube and ovary attachment showed dilated ducts lined by columnar epithelium, several of which showed papillary projections of their lining epithelium, possibly representing remnants of Gartner's ducts.

Sections of the other ovary showed corpora albicantia, numerous sclerosed blood vessels and small cysts with epithelial lining, apparently derived from old graafian follicles.

Sections of the appendix showed fecal material in the lumen, and the mucosa was lined by an intact layer of columnar epithelium. The interglandular stroma was infiltrated by mononuclear cells and occasional eosinophiles. The lymphoid tissue was fairly abundant and edematous, and occasional vessels on the serosal side were surrounded by lymphocytic infiltration.

*Pathologic Diagnosis.*—Papillary adenocarcinoma of the left fallopian tube, with associated hematosalpinx, chronic salpingitis, and perisalpingitis with adhesions. Chronic salpingitis and perisalpingitis of the right side. Bilateral chronic oophoritis with minute retention cysts. Atrophy of endometrium. Chronic appendicitis.

#### REFERENCES

- (1) Barrows, David N.: AM. J. OBST. & GYNEC. 13: 719, 1927. (2) Kahn, Milton E., and Norris, Samuel: AM. J. OBST. & GYNEC. 28: 393, 1934.

550 PARK AVENUE

---

Nizza, M.: The Influence of Local Thermo Therapy Upon the Temperature of the Deep Genital Sphere, Boll. d. Soc. piemontese di Ostet. e ginec. 2: 1086, 1934.

Using a thermoelectrical system the author studied the temperature in uterus, vagina, and rectum during the application of cold or heat to the epigastrium. The mean difference in temperatures was 0.26° C. He observed moreover how in some cases the deep temperature of uterus, vagina, and rectum was temporarily lowered by the initial application of heat and raised by cold.

AUGUST F. DARO.



## MONOAMNIOTIC TWINS, ONE NORMAL, THE OTHER ANENCEPHALIC; MULTIPLE TRUE KNOTS IN THE CORDS\*

SOL LITT, M.D., AND HERMAN A. STRAUSS, M.D., CHICAGO, ILL.

*(From the Department of Obstetrics, Michael Reese Hospital)*

MRS. G. S., a thirty-year-old para iv, entered the Michael Reese Hospital on May 17, 1935, on the service of Dr. R. Gordon. The pains started and membranes ruptured early in the morning of the same day. Her three previous pregnancies had been normal, as had the puerperium except for phlegmasia alba dolens and breast abscess after the third child.

The present pregnancy had been normal until four days before entrance, when fetal movements had no longer been felt and fetal heart tones could not be obtained. The patient would not be at term until June 22, 1935.

The patient entered the hospital at 11:45 A.M. with membranes presenting at the external os. Examination also revealed complete effacement and dilatation of the cervix and a breech presentation, as well as a knotted prolapsed cord. The prolapsed cord was not pulsating. Because of the inability to palpate the cephalic pole of the fetus, the possibility of the fetal deformity was considered. There was also considerable difficulty in outlining the fetal ovoid because the patient was very obese. The diagnosis of intrauterine death of the fetus with possible deformity was made.

At 12:05 P.M. a pulseless cord was visible at the vulva, and at 12:10 a stillborn anencephalic male monster was born by the breech. The cord of this fetus was entangled and knotted with a second cord, and at 12:14 a second stillborn male fetus was born in cephalic presentation. The placenta was expressed at 12:20 P.M., and was complete and intact.

Examination of the specimen revealed a single placenta measuring 15 by 18 by 3 cm. with one chorionic and amniotic sac. The membranes were complete and intact, and there was no evidence of an amniotic partition on the fetal surface of the placenta. Two cords inserted into the fetal surface of the placenta in an eccentric position, and about 2 cm. apart. The cords were free for a considerable distance from the placenta (about 30 cm.) when they were entangled and knotted in multiple true knots. From the knotted area the cords separated again, each then leading to its respective fetus. One fetus was grossly normal in every respect, except for being approximately five weeks premature, and much macerated. The other fetus was a typical anencephalic monster, the cranial vault and contents being entirely absent. A glistening reddish membrane covered the base of the skull. There were no evident abnormalities of the spinal column, or of the rest of the body. The twins were of approximately the same size and stage of development, and there was no evidence of earlier death of either of them. The umbilical cord of the normal twin was wound once around the neck and once around the thorax (not shown in photograph).

### COMMENT

This case is of interest because of the relative rarity of a gross developmental anomaly of one twin, the other being normal. The literature makes but little mention of anencephalic and normal twins. DeLee<sup>1</sup> states that the same deformity

\*Presented at a meeting of the Chicago Gynecological Society, May 17, 1935.

often occurs in both twins, but does not speak of single deformities in twin births. The more common instances of *acardiacus* and *fetus papyraceus* are also noted by this author. Döderlein<sup>2</sup> makes similar remarks on the deformities arising from "asymmetry" in the placental circulation. These cases are, however, due to inequality in blood supply, the one fetus becoming parasitic upon, or compressed by, the other.

A further point of interest is in the multiple knotting of the two cords. It is probable that this knotting, together with the winding of the cord about the neck and body of the normal twin, was responsible for its death. Dietrich<sup>3</sup> has reported a case where entanglement and false knots of the cord tightened after the birth of the first twin, and led to the death of the second before delivery could be effected. It is doubtful that the anencephalic twin was capable of independent existence.

This case represents an instance of monoamniotic twin pregnancy, of which Quigley<sup>4</sup> has recently collected 109 examples from the literature. This author men-

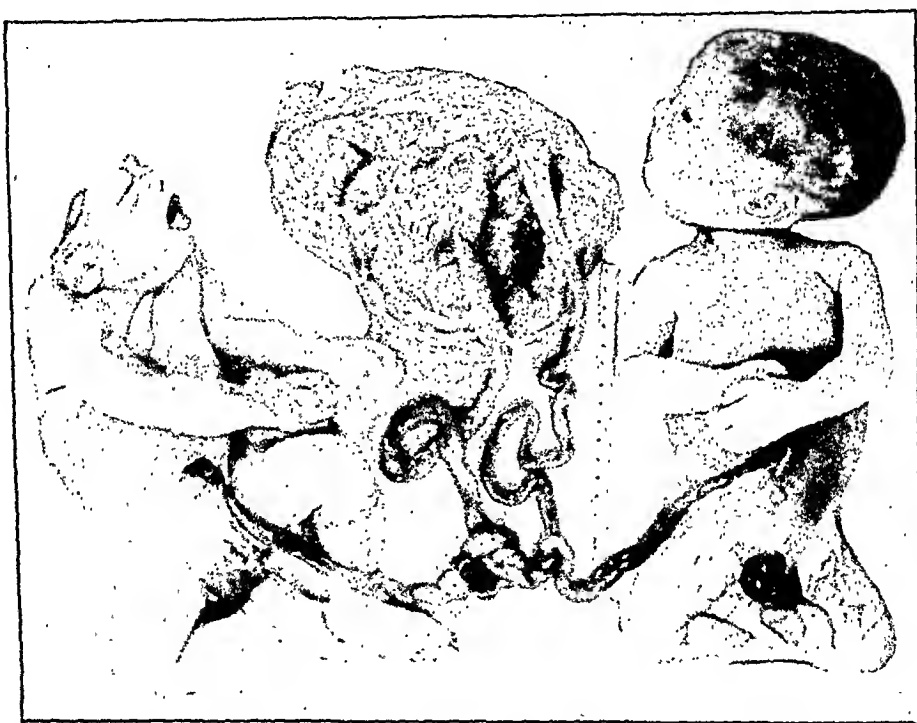


Fig. 1.—Monoamniotic twins, one (left) anencephalic, the other normal. Note multiple knotting of the cords, and absence of amniotic partition between the placental insertions of the cords. Cord of the normal twin was wound once about the neck and once about the thorax.

tioned 8 instances of monsters among the collected cases, but did not describe the types encountered.

There is a possible conformity of this case to the idea of Streeter,<sup>5</sup> that localized deformities in the fetus are due to disparity in the vitality of different tissues of the body. He states that there are found extreme disparities where the tissues have an anomalous excess of vitality and growth potency or in the other direction have decreased growth capacity leading to entire absence of a given portion of the body, there "being no evidence that even its primordium was ever present." Streeter believes that these defects are involved in the constitution of the germ plasm. In discussing a case of anencephalus under his observation, he concludes that we deal with defective development dating back to the time of formation of the amniotic cavity and the laying down of the germ disk, and that such defect existed before the appearance of the notochord and for that reason certain parts of it were not involved. He feels that one must assume that but a small portion of the

anterior part of the germ disk was affected in such a case of anencephalus, comprising the cells that form the oral end of the medullary folds and sparing the primordia of the eyes.

Such a view of localized developmental defects would seem to apply in this case, as otherwise explanation of anencephalus in one of identical twins, the other being structurally normal is difficult to provide. It would seem that a disparity in the vitality of certain structures in one twin could occur locally, resulting in anencephaly, whereas the other twin might not be so affected, and would go on to normal development.

Acknowledgment is made to Dr. R. Gordon for permission to present this case.

#### REFERENCES

- (1) *DeLee, J. B.*: Principles and Practice of Obstetrics, ed. 4, Philadelphia, 1925, W. B. Saunders Co. (2) *Döderlein, A.*: Handbuch der Geburtshilfe, Munich, 1915, J. F. Bergmann. (3) *Dietrich, S.*: Zentralbl. f. Gynäk. 38: 587, 1914. (4) *Quigley, J. K.*: AM. J. OBST. & GYNEC. 29: 354, 1935. (5) *Streeter, G. L.*: Contrib. Embryol. 22: 1, 1930.

185 NORTH WABASH AVENUE  
104 SOUTH MICHIGAN AVENUE

## CHORIONEPITHELIOMA FOLLOWING FULL-TERM PREGNANCY\*

### A CASE REPORT

CLIFFORD B. LULL, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Pennsylvania Hospital)

CHORIONEPITHELIOMA is associated in most minds with hydatidiform mole, and although the literature shows that a certain percentage does occur after full-term gestation, nevertheless, inquiry among various members of this society elicited the information that very few had seen chorionepithelioma following normal pregnancy. Inquiry also among the larger clinics in the country, has failed to reveal a very frequent incidence. It was therefore thought advisable to report this case to call the attention to the fact that bleeding following pregnancy should be looked upon with suspicion. A search of the records of the Philadelphia Lying-In Hospital shows no case of chorionepithelioma following a full-term pregnancy. All cases of chorionepithelioma recorded followed abortions or hydatidiform moles.

Mrs. M. D., aged twenty-nine, first consulted me when she was approximately three months pregnant. She was a nulliparous patient who had had influenza in 1918, tonsillectomy in 1926, and an appendectomy in 1928. There were no other serious illnesses or operations. Her periods had been established at the age of fourteen; had always been regular; normal in amount and duration. Her last period was Dec. 26, 1933, and her expected date of confinement, Oct. 2, 1934. This patient was seen with regularity during the rest of her pregnancy, and at no time had any disturbing symptoms more than the usual discomfort associated with pregnancy. Her blood pressure, urine, and other findings remained essentially normal.

She was admitted to the Lying-In Hospital private service on Oct. 5, 1934. Her pains began at 5 P.M. and at the time of admission, were approximately five-minute intervals, lasting from twenty to thirty seconds. Fetal heart sounds were heard in the right lower quadrant and were of good quality. The blood pressure was 110/50.

\*Presented at a meeting of the Obstetrical Society of Philadelphia, May 2, 1935.

Labor progressed normally and at 9 P.M. she was given vi gr. nembutal and 1/150 gr. of scopolamine. The scopolamine was repeated at 1 A.M. Analgesia was good, and at 4:30 A.M., Oct. 6, 1934, the head was presenting at the vulva in R.O.A. position. Under light gas anesthesia, a median episiotomy was done and the head was lifted off the perineum. Duration of gas anesthesia was twenty minutes. The third stage was uneventful, the placenta being delivered sixteen minutes after the baby. The usual erantín and infundín were given. The child was normal and was sent to the nursery in good condition. The patient's puerperal period was uneventful. At no time during her confinement to the hospital, which lasted eleven days, was there any elevation of temperature or pulse. The perineum healed immediately and the lochial discharge was normal on all occasions. Both mother and child were discharged in good condition on Oct. 17, 1934. The patient was told to report for follow-up examination in four weeks, and her postpuerperal care was outlined before discharge.

The subsequent convalescence was normal until Nov. 7, when the patient began to bleed rather freely. She was put to bed, oxytocic drugs were administered together with sedatives, and in two or three days the bleeding stopped. No pelvic examination was made at that time. The patient again resumed her household duties which were limited to caring for the child and very minor household details.

On the thirteenth of November a sudden hemorrhage occurred, which was severe. She was immediately hospitalized, and at the time of admission she was in very slight shock. Intravenous injection of glucose together with stimulation was ordered, and the vagina packed temporarily. Six hours later, when the pulse and temperature were normal, she was taken to the operating room and under light gas anesthesia the vaginal packing was removed. The cavity of the uterus was explored with a blunt placental forceps and a few small shreds of decidual tissue removed. Examination under anesthesia showed involution of the uterus to be normal, and no adnexal masses. The uterus was packed, together with the vagina, and the patient returned to her room in good condition. The blood count the following day showed 64 per cent hemoglobin and 3,000,000 red cells. The packing was removed at the end of thirty-six hours. There was no further bleeding and on November 22, she was discharged in good condition.

While in the hospital her secondary anemia was actively treated. She remained in bed from the time of her discharge and was not seen until November 29, one week later. At that time her pulse was running between 90 and 100, and her temperature was normal. But during the entire week at home there had been a slight bright red bloody discharge. As this seemed to be rather unusual, she was again admitted to the hospital, and examined under nitrous oxide anesthesia (this patient was very difficult to examine without an anesthetic). During the course of the examination there was a spurt of bright red blood from the uterus, so that the uterus was again packed to control the bleeding. The examination revealed no pathology that was palpable in the pelvis and the uterus was well involuted. Chorionepithelioma was suspected and a Friedman test taken at this time was shown to be positive in dilutions of 1 to 20.

The quite typical elevation of temperature occurred the following day and immediate operation was postponed while the patient was given transfusions and other supportive treatment. There was no further hemorrhage when the packing was removed.

Five days later, in spite of an elevation of temperature and pulse, under light nitrous oxide and ether anesthesia, the abdomen was opened. The uterus was small and firm. Over the right horn there was a slight adhesion between the omentum and the peritoneal covering of the uterus. Upon lifting the omentum up, a small area about one-fourth inch in diameter was found with a bluish discoloration, and the peritoneal covering of the uterus almost perforated. Panhysterectomy was done as rapidly as possible and the patient left the operating room in good condition. Post-

operative convalescence until December 23, was more or less uneventful. The temperature receded and the pulse came down to about 90. The wound healed by primary union, and there was no unusual abdominal symptoms.

On December 30, sixteen days after operation, the temperature was normal and the pulse 96. On December 31 the patient began to cough and had definite pulmonary signs. X-ray of the chest on Jan. 3, 1935, by Dr. Paul Bishop, showed a great deal of mottled infiltration throughout both lungs, but more extensive on the right side and especially marked at the right base. His opinion was that this was a metastatic lesion. Reexamination on January 8 showed a distinct increase in amount of lung infiltration. Dr. Bishop's opinion was that the major portion of the pulmonary lesions was metastatic in origin. Patient's condition became gradually worse and by January 11, had definite signs of metastasis to the brain.

Death occurred on Jan. 13, 1935. Autopsy was not permitted.

Pathologic examination by Dr. John Bauer showed the uterus to be normal except in the region just anterior to the right horn where the surface was of a dark reddish blue color and the tissue definitely fatty. Here also there were two hemispherical nodules projecting above the surface of the organ. One of these nodules, the smaller, was 8 mm. in height and measured 12 mm. in diameter. The top was very soft and brown as though necrotic. There was also a firm pinkish nodule 4 mm. in height and diameter projecting from the upper surface of the right tube just proximal to its fimbriated end. The mucosa of the cervix and of the lower third of the uterus was normal in appearance. Microscopic examination showed a typical chorionepithelioma.

1731 PINE STREET

---

## SPONTANEOUS EVOLUTION OF A TRANSVERSE PRESENTATION\*

WILLIAM G. FRASER, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics, Norwegian Hospital)

TRANSVERSE presentations are of occasional occurrence, the statistics showing that in about one case in 200, the shoulder presents. Transverse presentations which correct themselves spontaneously are of exceedingly rare occurrence, this happening about once in 5,000 cases.

The case to be presented is of particular interest in that the baby weighed 3,262 gm., this weight being exceeded in the cases in the literature, by that of Busch 3,500 gm., and that of Herrgott 3,300 gm. Moreover, the entire mechanism was completed in forty minutes.

Mrs. D., forty-two years old, a white female, para viii, was admitted to the Norwegian Hospital at 2:00 A.M., Sept. 8, 1933, in labor. Her previous pregnancies, with the exception of the last, had all terminated spontaneously and each puerperium was afebrile. The one abnormality was a placenta previa lateralis, treated by rupture of the membranes and subsequent spontaneous delivery.

The patient's antecedent history was essentially negative and had no bearing on the case. Last menstrual period Nov. 17, 1932. Calculated term, Aug. 24, 1933.

She had had no prenatal care, but upon the onset of labor, at 9:00 P.M., called her local doctor who examined her vaginally, ruptured the membranes artificially, and then with obvious excitement, told her that something was wrong, and suggested hospital-

---

\*Presented at a meeting of the Brooklyn Gynecological Society, April 5, 1935.

ization. An ambulance was called, and the examination by the ambulance surgeon at that time showed the patient in active labor, a transverse presentation, fetal heart sounds absent, and by rectal examination, the presence of a hand prolapsed through a cervix 4 to 5 cm. dilated.

Upon admission to the hospital, the routine physical examination revealed no gross abnormalities in the cardiovascular, respiratory, or nervous systems. Abdominal palpation showed strong abdominal musculature, absence of either fetal pole in the fundus, a head lying in the right iliac fossa, the breech lying in the left iliac fossa, and the fetal back directed anteriorly.

The pelvic measurements were normal.

A vaginal examination revealed a prolapsed left hand through the cervix, which by this time was almost fully dilated. A loop of the umbilical cord was also prolapsed. This was not pulsating.

A diagnosis of right acromio dorsal, anterior position, with prolapsed left hand and cord and dead baby was made. A podalic version was suggested.

However, the uterine contractions then increased both in intensity and frequency, and the patient in spite of being cautioned, began to bring her voluntary muscles into play. The result was that after a few contractions, the prolapsed left hand appeared at the vulva and with each succeeding contraction, more and more of the arm became visible, until the left shoulder slipped into view from beneath the symphysis. Then, still under the influence of the strong uterine contractions, the child began to rotate upon its vertical axis, the head moving from the right iliac fossa anteriorly until it came to rest overriding the symphysis pubis, and the breech moving posteriorly until it came to lie in the region of the promontory.

With the angle between the shoulder and the neck (which by this time had become considerably elongated) remaining the fixed point, the uterine contractions produced an extreme lateral flexion of the trunk, with the concavity directed toward the direction of the prolapsed arm. With descent into the pelvis being forced by the strong uterine contractions, there resulted, with a movement similar to extension in an occiput anterior presentation, first the left lateral aspect of the thorax followed by the left lateral aspect of the abdomen, and finally the left buttocks protruded from the vulva.

A second rotation now took place, the body rotating anteriorly through 90 degrees, so that both buttocks presented at the vulva.

The next contraction produced the delivery of the breech. An examination to determine the cause of delay following this revealed that the right arm had become extended over the head. This was swept down over the face, and with the use of the Mauriceau maneuver, aided by suprapubic pressure, the head was delivered.

There were no lacerations. The placenta separated spontaneously ten minutes later and was expressed by a modified Credé. The blood loss was 300 c.c.

The entire mechanism, from full dilatation to the delivery of the placenta, occupied only forty minutes. The baby was stillborn. It weighed 3,262 gm. There was nothing corresponding to a caput succedaneum on the shoulder that was prolapsed. The neck was elongated, and the head inclined toward the right shoulder. The upper part of the chest showed numerous ecchymoses. Autopsy of the baby was refused.

The puerperium was uneventful, and the patient was discharged on the tenth day after an uneventful uncomplicated convalescence.

## BRENNER TUMOR OF THE OVARY\*

PHILIP HAMBLIN SMITH, M.D., F.A.C.S., EVANSTON, ILL.

(From the Department of Obstetrics and Gynecology, Evanston Hospital)

THE patient, a widow, aged forty-five, was first seen in February, 1935, at which time she gave the following history: One pregnancy carried to term and delivered normally fourteen years ago. Menses began at thirteen and have been regular every twenty-eight days until three months ago when they began a week early and with a considerable increase in flow. The two subsequent periods were likewise excessive in amount. She has had no operations and denies disease other than measles and influenza.

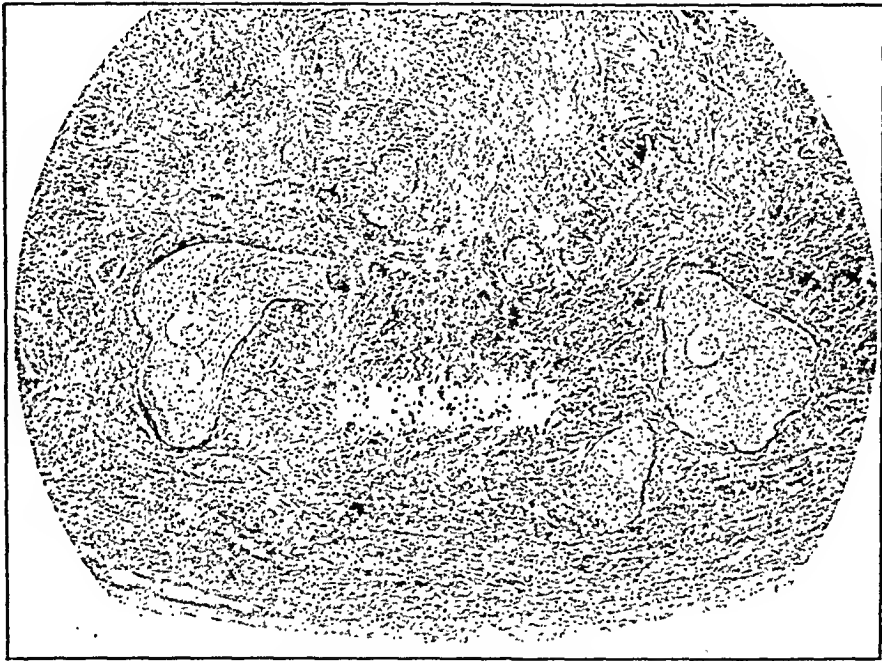


Fig. 1.—Showing coarse interlacing bundles of fibrous connective tissue and two nests of epithelial cell masses with their cystlike cavities containing "foam cells."

She presented herself at this time because of this increase in menstrual flow and what she described as a tight feeling in the pelvis.

Examination revealed a moderately relaxed vagina. The cervix was normal. The uterus was anteflexed, very irregular, mobile, and three or four times normal size. The right ovary seemed some larger than normal. The left adnexa were negative.

The Wassermann and Kahn tests were negative.

The urine was normal. The blood count showed 4.14 red blood cells, 8,500 white blood cells, and hemoglobin was 65 Sahli units.

*Operation.*—April 3, 1935. Median laparotomy. The uterus was found to be four times normal size and contained numerous subserous fibroids. The right ovary was three times normal size and contained a mass resembling a fibroma. Gallbladder and appendix were normal.

\*Presented at a meeting of the Chicago Gynecological Society, May 17, 1935.

Subtotal hysterectomy with removal of the right adnexa was done.

The postoperative course was uneventful and the patient was discharged on the fourteenth postoperative day.

*Pathologic Examination (Microscopic).*—Sections of the ovarian tumor show a structure which is predominately fibrous but which contains numerous thick cords and nests of large, polyhedral, epithelial cells. These cells are pale with distinct cell outline and almost clear cytoplasm. Their nuclei are oval, pale, contain small, dark nucleolus and a few fine granules of chromatin and occupy about two-thirds of the cell. Few mitotic figures are seen and the cells are remarkably uniform in size and staining reaction. A few of these cell masses contain one or more minute, cyst-like cavities, incompletely filled (shrinkage) with lipoid-laden "foam cells" and granular detritus. These cavities are apparently formed by fatty degeneration of centrally located epithelial cells since evidence of such degeneration is seen in other cells bordering on the "cysts." No true alveolar structures are seen in any part.

The stroma which constitutes over nine-tenths of the tumor consists of coarse anastomosing and interlacing bundles of fibrous connective tissue. A section through the ampulla of the tube shows two small compact masses of epithelial cells, similar in every respect to those of the ovarian tumor, which are embedded just beneath the peritoneum on the anteligamentous surface.

*Diagnosis.*—Encapsulated "follicular oophoroma" (Brenner) of the ovary. Minute "oophoroma" nodules on the surface of the fallopian tube. Adenomyomatosis of the uterus. Premenstrual hyperplasia of fundic endometrium.

636 CHURCH STREET

---

**King, Arthur G.: The Friedman Rabbit Ovulation Test in Differential Obstetric Diagnosis, J. Lab. & Clin. Med. 19: 1033, 1934.**

The author has collected 4,515 cases of Friedman tests from the literature to March, 1933, and has added 86 cases of his own. The gross error is 3.9 per cent. The false negative findings he divides into three classes: 82 due to limitations of the test, 13 to technical flaws, and 54 cannot be explained. The latter group with 26 false positive findings makes an error of 1.8 per cent. There were 48 cases in class three in the author's own series where early tests were negative while later tests were correctly positive. In 7 cases reported, the test was negative until the fourth to the sixth month. Therefore, a negative reading does not rule out early pregnancy.

In ectopic pregnancy a positive reading indicates that live chorionic tissue has been in existence within the last seventy-two hours; a negative test means little. Of 57 ectopies reported only 41 gave positive reactions and the author adds 2 in his own series. In hydatid mole and chorionepithelioma, perfect satisfaction is given in all reports. Carcinoma of the uterus occasionally gives a positive Aschheim-Zondek test although usually a negative Friedman test. One case in the series was negative and another positive (acanthoma). In obese patients, for the differential diagnosis between fibroids, ovarian cyst, and pregnancy, the test was very helpful. There were 13 such cases all correctly positive or negative, as proved subsequently. The author concludes that the test is a valuable aid in diagnosis provided its limitations are recognized. A positive test indicates usually, but not always, the presence of live chorionic tissue. It may not become positive until pregnancy is well advanced, and if positive may not necessarily mean that the fetus is alive. The test should assist but not supplant the usual diagnostic technic.

W. B. SERBIN.



# Society Transactions

---

## AMERICAN GYNECOLOGICAL SOCIETY

### SIXTIETH ANNUAL MEETING

*Hot Springs, Va., May 27, 28, 29, 1935*

The following papers were read and are published in the Journal, except as noted. Abstracts of the discussions are presented and the complete proceedings will appear in the current volume of the Society's Transactions. The President, Dr. Brooke M. Anspach, of Philadelphia, Pa., was in the chair.

1. **Further Studies on the Mechanism of Labor by Means of the Roentgen Ray.** Drs. William E. Caldwell, H. C. Moloy, and D. Anthony D'Esopo, New York City. (For original article, see December issue.)

2. **Clinical and Bacteriologic Observations in Trichomonas Vaginitis.** Drs. Edward Allen, Lloyd B. Jensen, and I. H. Wood, Chicago, Ill. (By invitation.) (For original article, see page 565, October issue.)

### DISCUSSION

DR. CARL HENRY DAVIS, MILWAUKEE, WIS.—The typical vaginitis may be the result of a symbiosis since we consistently find both trichomonas and some type of streptococcus.

If we follow up the obstinate cases, as Dr. Allen has done, we are going to find that a high percentage of these constantly recurring cases must be ascribed to the male prostate as a possible source of reinfection.

Unless we get at the original source we will not clear up the infection in some patients regardless of the type of local treatment. I believe that local treatment should be kept up almost daily for the first week or two, and then be tapered off gradually. Some type of home treatment is necessary. There are a number of new preparations which have some advantages over the earlier forms of treatment.

DR. NORMAN F. MILLER, ANN ARBOR, MICH.—Our experience with this type of vaginitis coincides with that of Dr. Allen. Most of the patients respond to some form of local therapy. We have not, however, noticed any severe urinary symptoms except in the presence of an active vaginitis. Neither have we noticed any disturbance in menstruation which we felt could be attributed to trichomonas infestation.

The specificity of the flagellates in trichomonas vaginitis has often been questioned. The possibility of symbiosis has been mentioned frequently. Bacterial association to the extent of true symbiosis is not uncommon. It is known for example that anerobic microorganisms are able to live in the presence of air if they are permitted to grow in association with aerobic microorganisms (tetanus bacilli when grown with diphtheria bacilli). Whether the disease under consideration is an example of a true symbiosis between flagellates and streptococci remains to be seen. While this work strongly suggests such relationship, caution is necessary for nonsymbiotic

association of organisms is common. Furthermore, the normal vagina may harbor streptococci of various strains including the viridans.

The presence of trichomonas in the male urinary tract occasionally has been noted. One patient seen in the genitourinary service in our own hospital had a severe pyelitis apparently due to trichomonas. Unfortunately no cultures were made, but in the light of the work just reported, it is possible that streptococci were present as the fundamental cause of the kidney infection. Isolation from the male urinary tract of streptococci similar to those associated with the flagellates in trichomonas vaginitis strongly adds to the evidence of a true symbiosis.

The occurrence of cellulitis in several of these patients is extremely interesting. It seems logical that this should be due to the associated streptococci, but I wonder why it does not happen more frequently. Many of my most severe cases have been in pregnant women. If further study convinces Dr. Allen and his colleagues that the *Streptococcus viridans* is a necessary factor in trichomonas vaginitis, the potential seriousness of this condition as a complication of pregnancy is at once apparent.

DR. JOSEPH B. DELEE, CHICAGO, ILL.—I would like to emphasize the necessity of building up the general system of the patient in trying to cure trichomonas. I cured three patients permanently by giving thyroid. The basal metabolism was found to be very low and within three weeks there was a marked change. That was five years ago, and they have remained cured.

The study of the husband in these cases is important when one considers the intimate relations present.

DR. GEORGE GELLIORN, St. Louis, Mo.—It seems to me that clinical observations do not bear out the assumption that it is a streptococcus rather than the trichomonas which causes the condition under discussion. That assumption which has been made repeatedly in the past was based upon a statement accredited to Donné, of France, the discoverer of the trichomonas. In his original communication published in 1836, it will be noted that he did not find these trichomonads in the normal vagina as harmless parasites but only in purulent discharge. It would therefore appear that the trichomonas is the primary cause of the irritation, and that this irritation activates the ubiquitous streptococcus in the vagina and then gives rise to the complications mentioned by the speaker.

Another proof that this vaginitis is due to trichomonas is the result of treatment. The therapy initiated by Hoebe, of Germany, some twenty years ago has, with minor changes, been used until recently. It consisted in washing, and sometimes even scrubbing, the vagina with soap and water and then flooding it with a bichloride solution. This old method is extremely unreliable and in many instances has to be continued for months. The reason for this is clear. Were the streptococcus the causative agent, one or a few bichloride applications would kill or weaken the bacteria. The trichomonads, on the other hand, are not affected. Only when I introduced an entirely new principle into the therapy by insufflating an amebacidal specific into the vagina, an arsenical which affected only the trichomonads but not cocci, were the results changed. In very favorable cases the discharge would disappear overnight, and in the large majority of instances only three or four treatments were required to produce cure.

The prevention of trichomonas vaginitis is also pertinent to the subject. It has been claimed that these amebas came from the rectum, although there were some questions raised because the rectal and vaginal trichomonads were supposed to differ in the number of flagella. I am not competent to say whether this distinction is true nor am I prepared to say whether prophylactic oral administration or rectal enemas containing stovarsol have any protective value; but in at least one case of frequent

recurrences I could determine definitely that each return of the trichomonas vaginitis followed an intestinal upset and attack of diarrhea.

DR. FRED L. ADAIR, CHICAGO, ILL.—The few remarks I have to make are based on the work of Dr. Hesseltine at the Chicago Lying-In Hospital, who has been interested in infections of the lower genital tract for some time past. There are several etiologic factors which appear to be of great importance. First, it must be recognized, I think, that the trichomonas are not found in association with normal vaginal flora, that there are other associated bacteria. These associations are practically constant and this is emphasized by the fact that so far it has been apparently impossible to culture the trichomonas isolated from other bacterial forms. Perhaps this is explained by the supposition that other forms of bacteria are needed, so that apparently bacteria other than the normal bacteria of the vagina are necessary for the development of the trichomonas. Furthermore, the hydrogen ion concentration is altered in this type of infection. The histology also becomes important; apparently from the more or less mechanical alteration and the breaking down of the normal epithelium, with alteration in the cells themselves, the invasion of infective agents is rendered possible. By removing small pieces of vaginal tissue with a punch we find that there is a loss of epithelium. We find definite inflammatory reactions in the subepithelial or submucous layers. In association with this we have not been able to demonstrate the trichomonas in the tissue but have been able to demonstrate bacteria, indicating that the bacteria themselves are invasive rather than the trichomonas. Third, by the alteration in the tissue chemistry itself, apparently in the lowering of the glycogen.

Treatment has been based upon the supposition that one could destroy these organisms by antiseptics, also by the use of coagulants, which would tend to increase the surface resistance; also by changes in the hydrogen ion concentration of the vaginal secretion; also by filtrates and other means of increasing general or specific immunity.

In the treatment we have tried innumerable things. Control methods were used, and it was found that apparently sodium bicarbonate by altering the pH of vaginal secretion seemed to work equally well as the stovarsol, so it was concluded that the latter was not necessary.

Stimulation of the growth of the normal vaginal bacillus is important in checking these infections, and this can be done by increasing the carbohydrate content of any agent which is applied to the vagina. Inasmuch as these infections are common and no form of yeast ferments lactose, it has been selected as an agent which favors the growth of the vaginal bacillus which tends to increase the sugar content of the vaginal epithelium and also tends to restore a normal pH in the vagina. By combining citric acid with lactose 5 per cent and 95 per cent respectively, favorable results have been obtained.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—There can be little doubt that behind every case of trichomonas vaginitis, there is an individual susceptibility, as in all other infections.

In many instances of this disease, local treatment, however prolonged, may not produce a cure, until some elevation of the general tone of the body is brought about by appropriate remedies. In one instance, large doses of iron, in others, sun treatment, proved efficient when combined with topical care.

In my experience, there have been recurrences due to prostatic trichomoniasis in the husband. But that this is not a common source of infection is proved by the frequency of the disease in young virgins. That contact is a fruitful cause of spread is shown by the incidence of the same disease in two or three members of the same family, chiefly children.

I have studied the variations and find certain morphologic differences as shown in Fig. 1. *A*, shows the type of trichomonad usually found in the ordinary case of vaginitis. *B*, shows the rarer type, which I have called the "windmill"; the flagellae which are grouped at one end spin very rapidly. The "angler," is a much rarer form, found only twice in over 300 cases. The organism operates this flagellum rhythmically, and as perfectly as an angler casts his "fly." The movement is never fast, but almost deliberate. It slows perceptibly on cooling. The end of the flagellum is armed with a nob. Whether this is a sneaker or not, cannot be detected. The "spin-wheel," having all its flagellae beating in one direction, spins about rapidly thereby causing currents to approximate food. The "seal" is the most interesting of them all. Its larger base is more or less fixed to the substance on which it rests, but its upper half is as mobile as the head of a seal, and closely resembles the latter in all its movements. Whether these forms are conditioned by soil and food is at present impossible to determine. But whatever the cause, mixed types are not found in the same clinical case. Though the organisms may vary much in size in the same case, they are true to type. This rather leads one to believe that at least the types described are generic rather than developmental. The

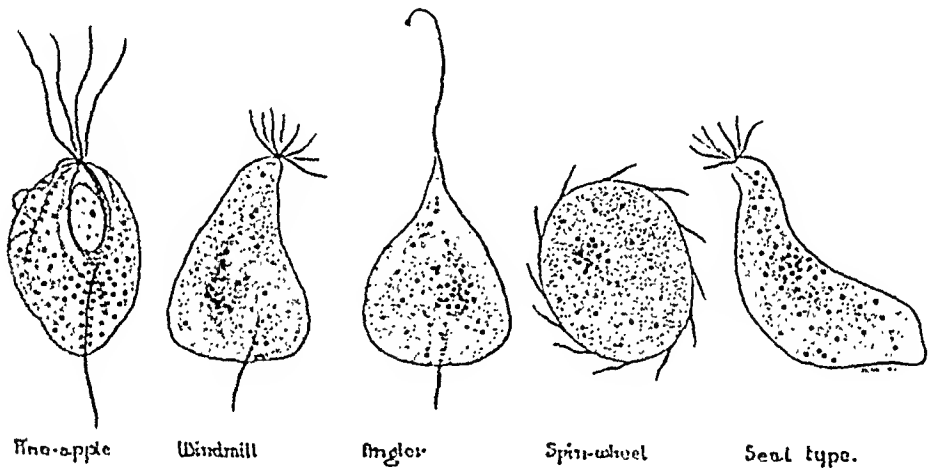


Fig. 1.

corporeal properties of the different types of trichomonad seem fairly uniform, but the differences are chiefly in the distribution of the flagella, whose functions seem to be both auto- and circumferential locomotion for procuring sustenance.

DR. ALLEN (closing).—I am very much interested in the discussion of the types of trichomonas that Dr. Goodall has shown. I wonder if these various forms of trichomonas are not similar to the change in form of the streptococci? When these organisms are cultured they assume a great many diverse forms and I wonder if this change in type or structure of the trichomonas may not be due to changes in the habitat?

The report of Dr. Adair that there were organisms in the subvaginal tissue is very interesting, especially in association with the bladder symptoms. Recently we have been cystoscoping these patients and quite a number of these women, even without urinary symptoms, have a condition that resembles inflammation in the trigone. We have also noticed in several, little petechial hemorrhages scattered over the fluffy, edematous bladder mucosa.

Replying to Dr. Gellhorn, I did not mean to say that these organisms are the cause of the condition. I just wanted to report their association with trichomonas.

#### 4. The Treatment of Dysmenorrhea by Presacral Sympathectomy. Dr. Floyd E. Keene, Philadelphia, Pa. (For original article, see page 534, October issue.)

##### DISCUSSION

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—I believe it important to call attention to one phase of dysmenorrhea which should be considered before such an operation as presacral sympathectomy is performed.

It is known that essential dysmenorrhea in a considerable percentage of cases is due to allergy. In 1931, D. R. Smith, my associate, reported 12 cases: 8 of the patients were cured completely by withdrawal of the food to which these patients were sensitive. There were 4 partial cures. Since that time Smith has had 10 more patients who are entirely free of symptoms since the allergic factor has been withdrawn. In 5 other cases there was definite improvement, and there were also 5 failures. With these figures in mind, I think it is very important to rule out allergy before any radical operative procedure is carried out.

DR. CHARLES A. BEHNEY, PHILADELPHIA, PA.—About four years ago I began to perform this operation for patients with intense pain from carcinoma of the cervix. About three years ago we started to do some sympathectomies for dysmenorrhea and since that time have operated upon eleven patients, with four failures in securing complete relief. Sometimes we learn more from our failures than from our successes, and I feel that in these instances complete relief would not have been expected had they been thoroughly studied from urologic and orthopedic standpoints. This operation is indicated only in the type of dysmenorrhea that has been studied from every standpoint and cannot be cured by more conservative measures. There are patients who have pelvic pain due to lesions of the pelvic sympathetic nerves and who can be relieved only by excision of these structures.

The longest permanent relief which we have secured has been for three years.

DR. EMIL NOVAK, BALTIMORE, MD.—While I have performed this operation in only a few cases, it impresses me as a valuable addition to our armamentarium in the treatment of cases of very severe primary dysmenorrhea in which other measures have been unsuccessful.

The psychic factor is such an ever present one in the evaluation of treatment in cases of dysmenorrhea that one cannot set it aside in appraising the results of presacral sympathectomy. However, when one stops to think that this procedure is apparently capable of relieving the very genuine and very severe pain of advanced malignancy, there would seem little justification for skepticism as to its possibilities in dysmenorrhea. One would think that the operation would be hailed with delight, offering as it does a logical and yet not too radical means of treating the occasional severe and intractable case where constitutional, psychotherapeutic and other measures have been without avail.

Technically the operation may be looked upon as a rather simple procedure, and when properly done, apparently producing no harmful effects. Where unusually severe dysmenorrhea is the chief symptom of otherwise unimportant pelvic abnormalities, such as displacements, so that there is some doubt as to whether correction of the latter will relieve the severe pain, presacral sympathectomy may well be combined with other operative measures, such as suspension, which may be indicated.

#### 5. A Study of a New and Potent Ergot Derivative. Drs. Fred L. Adair, M. Edward Davis, M. S. Kharasch, and Romeo R. Legault, Chicago, Ill. (For original article, see page 466, October issue.)

## DISCUSSION

DR. M. PIERCE RUCKER, RICHMOND, VA.—In 1921, Dr. Haskell and I became very much interested in the action of pituitrin, and one method of approach was to compare it with the action of ergot. We tried three different preparations, the fluid extracts and two so-called purified preparations. We tried them on isolated strips of uteri and also upon uteri intact in dogs and cats, and in two instances I tried it antepartum with a bag in the uterus, also in a number of cases after the third stage of labor using the external method of Rübsamen. Our results so far as ergot was concerned were extremely disappointing. In the first place we could not standardize preparations of ergot, and it was necessary to use, in order to get any effect on the animal's uterus, as much as twenty times the amount of ergot as of pituitrin, and in some cases as much as thirty-two times the amount of pituitrin. The effect on the human being was even more variable. In the antepartum cases I could get no appreciable effect, although there were only two. In some cases immediately postpartum we could get some demonstrable results with as much as one or two drams of fluid extract of ergot, but it was not as successful as pituitrin.

With regard to the method used by Dr. Adair, Koff several years ago stated that he thought that the immediate use of a bag postpartum was a dangerous thing; in a previous communication I think Dr. Adair used the bag immediately after the third stage of labor. In the present paper I believe he has recommended it after the fifth or sixth day. I am wondering if he found any bad effects from this method when used immediately after delivery?

This work is most important both as to the method used and because Dr. Adair has given us a very reliable and constant ergot preparation. I have not yet been able to test it out with laboratory methods but clinically it seems to work very well indeed. I have used it immediately after delivery of the placenta. The uterus becomes extremely firm and stays so for several hours after delivery. It gets rid apparently of that secondary oozing that one often finds after putting the patient to bed after having given her a dose of pituitrin.

DR. ADAIR (closing).—Naturally there are many things in the paper which I did not have time to present today. We have used this method during labor, and we do use it immediately after the first stage, but for the most part our studies have been on the sixth to the eighth day postpartum uterus, and I might say that our cases have been selected with extreme care. We have used only multiparous women where there has been no morbidity. In over 200 cases there were no complications which one might apprehend. We did not inject this without some apprehension and have maintained, as I say, a very careful selection of the cases, with scrupulous technique.

Our conclusions are that we have isolated in crystalline form the active principle of ergot which is responsible for most, if not all, of the desirable oxytocic effect of ergot. We have designated this substance as ergotocin. It is potent in minimal doses by various methods of administration. It does not deteriorate readily and is constant in its action. It is relatively free from untoward or undesirable effects. Its margin of safety is very great as the degree of toxicity is very low. It has no apparent detrimental effects upon respiration, pulse, blood pressure, or urinary output. This emphasizes the value of its use in cases having evidence of cardiovascular-renal diseases or toxemias where oxytocic action is required. We are not advocating its use during the third stage of labor, but believe it may be used during this stage as safely and more effectively than any other known oxytocic drug. It is extremely valuable in stimulating uterine contraction in the immediate and remote postabortal and postpartum periods. Its prompt effect in producing tetany and contraction of the uterus, and its prolonged action, make it of special value in the management of postpartum hemorrhage. With the isolation of ergotocin, the age-

old problem concerning the oxytocic principle in ergot apparently has been brought to a close. We now have the desirable, potent, oxytocic activity in ergot isolated in a crystalline material, stable and nontoxic. Ergotocin can be used safely whenever an oxytocic therapy is indicated.

**6. Hypothyroidism as a Problem in Women.** Dr. Carl Henry Davis, Milwaukee, Wis. (For original article, see page 570, October issue.)

#### DISCUSSION

DR. L. A. CALKINS, KANSAS CITY, MO.—From our very limited experience of 126 cases it would seem that thyroid dysfunction is less frequent in Kansas City than in Milwaukee. Dr. Davis has very properly pointed out the necessity for the greatest of care in making the test as the results are materially affected by congestion of the breasts, mild uterine contractions, and other very minor disturbances. It is, therefore, not safe to depend upon the results as reported by the average laboratory technician.

In 126 cases we found 10 per cent above the normal range, 63 per cent within the normal range, and 26 per cent below the normal range. This latter group were all postpartum cases. None of the 126 received any treatment.

From this very limited experience we have two impressions with respect to the problem in the Kansas City area: First, that mild degrees of thyroid dysfunction may be contributory to certain of the variations commonly noted in labor and the puerperium; second, that the problem of thyroid dysfunction in the puerperal state is deserving of further investigation.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—I have been attracted to this disturbance in women from three standpoints: first, the standpoint of sterility and habitual abortions; second, the standpoint of various disturbances of menstruation; and third, the "general run down condition," as the patient usually calls it.

In 1926, I wrote on the subject of the relation of sterility to hypothyroidism and found in some seventy cases that 50 per cent of all sterile women had a low basal metabolism and by treatment with thyroid extract one-third of those women became pregnant. It should be remembered that we are in the goiter area the same as Milwaukee, and whether these things apply in the nongoiter areas I do not know. Of the unmarried women with low basal metabolic rate 40 per cent had disturbed menstruation.

In 1929, Dr. Carey cooperated with me in studying these cases from a medical standpoint, and we found in that series that 57 per cent of all women seeking help from sterility had a low basal metabolic rate and 37 per cent became pregnant after treatment with thyroid. Forty per cent in the first group had disturbed menstruation, and in this group 36 had a low basal metabolic rate; and 45 per cent as compared to 50 per cent in the previous group were sterile. Dr. Carey studied this subject from the standpoint of the internist entirely and in some 700 cases of women seeking advice for various disturbances found that 56 per cent of married women with a low basal metabolic rate were sterile. The average sterility rate is 13 per cent among American women. This work was summarized last year by Carey and Bromfield, both of the Nicollet Clinic. After summarizing the three previous papers of Litzenberg and Carey and adding the subsequent cases they found that 52.8 per cent of all the women had a low basal metabolic rate, and 39.7 per cent had menstrual disturbances.

The result of thyroid treatment of these conditions in the whole four series was that 34.3 per cent of the sterile women who had low basal metabolic rates,

became pregnant; and of all other symptoms for which they came, nervous disturbances, menstrual function, etc., 62.6 per cent were improved by treatment.

I have been particularly impressed by the fact that women on thyroid treatment even if they did not conceive were very much improved in their general health. We have had equally good results in women having habitual abortions; approximately 70 per cent with a low basal metabolic rate have been carried through subsequent pregnancies successfully. I agree with Dr. Davis that certainly in the goiter areas, basal metabolism rates should be taken frequently upon many gynecologic and obstetric patients. I do not do it routinely, but where there are certain indications it is done and in most of the cases of habitual abortion the patients carry through to full term. In 62 per cent of the women with menstrual disturbances they are improved or cured.

DR. PHILIP F. WILLIAMS, PHILADELPHIA, PA.—The explanation which Dr. Davis has given for the increase in the number of women with hypothyroidism in the Milwaukee area is intriguing. Presumably continued studies of the women in that district who have been subjected to iodine therapy during adolescence will confirm his explanation. The Atlantic seaboard did not suffer the destructive geologic influences of the Permian Age as did the Midwest, and consequently we do not have the same problem in and about Philadelphia as they seem to have in Milwaukee and adjacent areas. It is not surprising, therefore, that a cursory survey of the metabolic readings in two Philadelphia hospitals shows that less than 10 per cent have basal metabolic readings of lower than minus 15. Hypothyroidism is not a very frequent problem in obstetrics or gynecologic practice in Philadelphia, nor is hyperthyroidism, although we do have some instances in migrants. It is found sometimes in nervous, mental, cardiac, and anemic conditions and also in subnormal constitutional states. In Philadelphia we see low basal metabolic readings in sterile women and in some parous women with stillbirths. In some of these instances there may have been a deficient germ plasma in the hypothyroid woman. We have sometimes found that thyroid therapy stimulated the basal metabolic rate to a certain degree but did not bring it back to normal. In some of those cases pituitary preparations have been of assistance. Just what reference Collip's work bears to this problem is speculative.

So far as having a definite reading in basal metabolic studies, and as to what constitutes hypothyroidism, we believe that a woman with a minus 2 or 5 who is sluggish and easily fatigued is to be considered a hypothyroid case just as is a woman with a low basal metabolic rate, and they are often much benefited by thyroid therapy.

Three times I have seen craniorachischisis occur in fetuses of women with a low basal metabolic reading; in two of these cases the women conceived again and delivered normal children without any thyroid therapy.

DR. GRANISON D. ROYSTON, ST. LOUIS, MO.—Most internists attach little importance to basal metabolic readings of less than 20 per cent, yet I agree with Dr. Davis that there is a fairly large group of women, whose readings are not so low, who improve under thyroid medication. For some years I have been doing routine basal metabolism readings on all obstetric patients and on those gynecologic patients whose symptoms or physical findings suggested thyroid dysfunction.

Our findings agree fairly closely with those of Dr. Davis.

A group of 231 gynecologic patients studied by us, selected because of the suspicion of thyroid dysfunction, showed minus readings present in 74 per cent of this number. Because of their being in a selected group, this figure is not a fair index as to the frequency of low basal metabolic readings.



The basal metabolic readings in the last 419 consecutive obstetric patients showed 63.4 per cent were on the minus side; 23.8 per cent were minus 10 per cent or lower. Weight played but little part in the basal metabolic rate, since in only the group weighing from 150 to 159 pounds did the plus readings exceed the number of minus readings. I might add that height played no part in the basal metabolic readings.

We have attempted to classify these patients according to types: the asthenic type showing genital deficiencies as congenital displacements, retrocession, elongated cervix, infantile uterus, contracted pelvis (chiefly of outlet), etc., plus evidences of congenital tissue deficiency in other parts of the body, as the narrow high hard palate, narrow costal arch, diastasis, splanchnoptosis, etc. Where evidences of congenital tissue deficiency of parts of the body not including the genitalia were present, the individual was classed as hyposthenic. Sthenic types showed none of these deficiencies, and hypersthenic showed some exaggeration of the normally physically well-developed person.

Among the 231 gynecologic patients, 18 per cent were classed as asthenic; 48 per cent as hyposthenic; 31 per cent as sthenic and 2 per cent as hypersthenic.

The 419 consecutive obstetric patients comprised 9 per cent asthenic; 48 per cent hyposthenic; 37 per cent sthenic; and 6 per cent hypersthenic, suggesting that asthenic types are possibly less apt to conceive.

Fatigue was present in approximately 50 per cent of our patients while 20 per cent complained of mental depression. Less than 2 per cent of the patients in our series complained of somnolence, whereas 40 per cent suffered from insomnia.

We attach much importance to the basal pulse, which is counted at the time the basal metabolic reading is determined, and we feel that this basal pulse is second in reliability only to the basal metabolic rate itself. The patient is taught to count her basal pulse in the carotid artery on awakening, twice weekly, and we have found it a valuable aid in helping to regulate her thyroid dosage.

Those patients Dr. Davis mentioned as having low basal metabolic readings and a fast pulse, did not do well under thyroid in our series, possibly because we did not continue its administration long enough. However, we feel that these patients should have malnutrition excluded as a possible factor. Such patients did better with iodine and a high fat diet under our care.

Dr. Litzenberg has emphasized the importance of hypothyroidism in connection with sterility. In this series there were 70 sterile patients. Of this number, the male factor was present in 13; in 5 others we were unable to complete the examination. However, of the 52 remaining patients, 53.8 per cent conceived and the largest group of conceptions was treated solely with thyroid and a high vitamin E diet. Of the sterility patients who conceived, more than 82 per cent received thyroid medication.

DR. JAMES E. KING, BUFFALO, N. Y.—I feel from my own experience that too great stress has been laid upon the value of the basal metabolic rate. At first I was inclined to have all of my cases tested by this method and I found, much to my surprise, that even in cases where the basal metabolic rate was not disturbed, the use of thyroid benefited my patient. At present I am not using the basal metabolic reading but feel that we can by questioning our patients get enough evidence to indicate a thyroid deficiency.

I give larger doses of thyroid than Dr. Davis gives, usually a grain morning and night, and then as the symptoms improve or a change is noted upon examination, the dose is decreased or increased as needed.

DR. EMIL NOVAK, BALTIMORE, Md.—Attention may again be called to the very obvious fact that in thyroid studies in cases of sterility the male partner is entitled to the same consideration as the female. In a couple which I recently

examined, the wife showed a metabolic rate of minus 45, but that of the husband was minus 55.

I agree with the previous speakers as to the frequent value of thyroid medication, although we know little as to the nature of the thyrogonadal relationship. While, in my experience, hypothyroidism is more often manifested by excess rather than deficiency or absence of menstruation, there are so many exceptions to this rule as to confuse our ideas concerning the mechanism which may be involved. The same is true as regards hyperthyroidism, which most frequently is associated with menstrual deficiency rather than excess. Perhaps the thyroid rôle is only an intermediary one, the real disturbance involving the thyrotropic hormone produced by the anterior lobe.

Certainly in Baltimore and vicinity we do not find anything like as high an incidence of hypothyroidism with sterility as Dr. Litzenberg finds in Minnesota. As a rule the gynecologist is rather grateful if he finds a very low basal rate in the sterile woman, for a logical course of treatment is at once indicated, with frequent success. Even with a normal rate, however, the judicious use of thyroid is fully justified, not only in sterility, but often in cases of habitual abortion. Just how it acts in the latter group no one knows, though there is some reason to think that its effect is upon the germ plasma. Embryologists now accept the doctrine of defective germ plasma as a cause of "idiopathic" abortion.

There are some women who menstruate but do not produce ova, thus accounting for certain cases of sterility. There are others who ovulate, but in whom the ova are of poor quality, unable to combine with spermatozoa. These, likewise, are sterile. In others the egg becomes fertilized, but the germ plasma is so deficient in quality that the pregnancy "peters out" prematurely, and this may occur repeatedly, as in habitual abortion. In still others the pregnancy goes to term, but the child is born dead or dies soon after birth. Finally, in the ideal cell union, the *vis a tergo* is sufficient to carry the egg throughout the normal human span. It is perhaps an effect upon this elusive factor of germ plasma which thyroid therapy brings about, so that there is full justification for the inevitable "pinch of thyroid" commonly added to other efforts at organotherapy.

DR. FRED L. ADAIR, CHICAGO, ILL.—In habitual abortion I had a number of cases that responded to the administration of corpus luteum and I think it is possible that the administration of thyroid extract might operate on the corpus luteum and accomplish this result in a different way.

I should like to refer to the administration of iodine to the mother and its effect upon the fetus. A number of years ago Dr. George Hudson carried out some rather extensive experiments upon rabbits. Of course, if iodine does not pass through the placenta we would not expect it to affect the fetus. He was able to demonstrate that inorganic iodine did pass through the placenta and consequently we felt that the chances were that in the human being it also might pass through the placenta. Its influence was demonstrated by the presence in increased amounts in the fetuses of animals who received it as compared with animals that did not receive it. It was also demonstrated by histologic examination showing a difference in thyroid of those who received iodine and those who did not.

DR. ROBERT T. FRANK, New York, N. Y.—This does not seem to me a problem that can be settled by statistical methods. Sometimes we can get more information by a few cases rather than by statistics.

On the Atlantic seaboard a 10 per cent minus or plus basal metabolic reading ordinarily has little significance. If it is minus 10 it is more apt to be significant as the newness of the examination has a tendency to increase the rate and therefore

signifies more than a plus reading. I feel that repeated tests are necessary before we consider it a disturbance of metabolism.

I agree fully with Dr. Williams that these minus grades can usually be favorably affected by increasing the caloric intake, the protein rather than the fat diet.

Another startling thing, as Dr. Novak has already mentioned, is that you see both amenorrhea and particularly puberty bleeding in patients who have the same clinical manifestations, namely lowered basal metabolism. I am not speaking now of these minor deviations, but of a minus 20 or 30.

The response to thyroid therapy is gratifying. That leads you to conclude that probably the thyroid is simply an index of a deeper lying disturbance, otherwise it should not manifest itself in these two diametrically opposite fashions. Therefore, at the moment we are probably merely at the threshold of recognizing the single something which however is based upon a more fundamental underlying trouble and probably the prepituitary.

I do not believe that doses of thyroid of one-fifth of a grain can really have an influence upon a lowered basal metabolism. A reading of minus 10, 20, or 30 requires ascending doses. Furthermore, it should be kept well in mind that thyroid medication lasts only a short time. If the patient is given thyroid for four or five weeks consecutively and you stop for ten days, the thyroid effect is over and is not carried beyond that definite influence. So while the basal metabolic test—and I think it is far superior to any other method of recognizing thyroid overaction or underaction—is extremely important, it does not afford conclusive evidence as to the location of the underlying condition.

DR. DAVIS (closing).—I believe that we are all in rather complete accord regarding the use of thyroid. Reference has been made twice in the discussion to one-fifth of a grain. Apparently there is a misunderstanding. I mentioned the fact that if a patient had a reading of minus 10 and had symptoms which suggested that there might be some thyroid disturbance, I start out by giving one-fifth of a grain U.S.P. per day and in two or three weeks repeat the basal metabolism test. Some patients have been relieved of symptoms and continue to have normal readings thereafter. Others have been found on repeat tests to be in the minus 20 group or lower. The largest dose I am giving at the present time is  $5\frac{1}{2}$  gr. per day of the Burroughs-Wellcome thyroid.

Dr. King and I have reversed our ideas. For years I believed that it was possible for me from a clinical point of view to determine which patients should have a metabolism test. In the last year and a half I have had basal metabolism rate tests done on 600 consecutive patients and the results have convinced me that it is not possible by any method other than the basal metabolic reading to determine safely which patients may be benefited with the use of thyroid medication.

The purpose of this paper was not to show that the metabolism rate is low in the vicinity of Milwaukee, but to emphasize again the fact that the men doing obstetrics in this country are the ones who may keep our population from developing thyroid disease such as they have in Switzerland, Bavaria, and other places where the people have been living for a thousand years or longer in goiter areas. With the information available at the present time I believe it is possible to keep from ever having a serious goiter problem in this country.

MR. VICTOR BONNEY, of London, spoke on the **Extended Scope of Myomectomy**.

Too many hysterectomies for fibroids are being done at the present time. That the ideal of surgery should be cure without deformity or loss of function is a truism, but apart from this the value of the uterus from the psychologic point of view needs

careful consideration. Women vary in their reactions to hysterectomy, but there is a very definite proportion who take the loss of the womb very much to heart; either because they are aware that to many men the idea of a woman not being "whole" is unattractive, or on account of the irrevocable sterility.

Myomectomy in the past has had a definitely limited scope, being restricted to cases where the tumors were single, or if multiple then superficially placed. Resenting this restriction I have extended the operation until now I am able to perform it on any case of fibroids if in my opinion conservation of the uterus is desirable. Myomectomy thus extended in scope should be in the repertory of every surgeon practicing gynecology, thus enabling him to do the best for any particular patient instead of being compelled to do a mutilating operation against his inclination, as is still far too commonly the case.

In a general way my rule is that in patients under forty-one years of age the preferential operation is myomectomy, while in patients over that age hysterectomy should be chosen. There are, however, exceptions to the rule; on the one hand, the relatively young woman who having had sufficient children wants to have her womb removed, and on the other the elderly woman who for private reasons, sentimental or otherwise, desires its conservation.

I have performed myomectomy 487 times. The fibroids were solitary in 237 cases, and multiple in 250 cases. Of the multiple cases the largest number of tumors I have removed from a single uterus is 125, and after that 92, 90, 80, 56, 55, 52, and 50, and so on downward.

I have had 7 operative deaths, a mortality rate of 1.2 per cent. No deaths have occurred in my last 200 cases, owing to improved technic.

In a Hunterian Lecture given at the Royal College of Surgeons of England in 1932 I showed that new fibroids formed in 5 per cent of the cases, but only in 3 per cent to the extent of requiring further operation. All these cases were patients who had developed fibroids at an exceptionally early age and to whom, therefore, a special fibroid-forming tendency must be ascribed.

Of 77 women within the childbearing age who wished and were in a position to have children 30 (or 39 per cent) did conceive. Seventy-five per cent of the deliveries were normal and 25 per cent were by cesarean section. The high percentage of cesarean sections was due to the relatively advanced age of the mothers and the specially great obligation to deliver a living child.

In regard to the technic I employ, I lay first emphasis on the myomectomy clamp invented by me. This instrument controls both uterine arteries at once, and in addition stops the entire blood flow from coming up through the cervix. The result is that when in addition the ovario-pelvic ligaments are compressed by ring forceps the circulation through the uterus is completely stopped and the operation becomes bloodless. The myomectomy clamp should be applied from the front at about the level of the internal os, and its grasp should include the round ligaments, for otherwise there is a tendency for the jaws of the clamp to slip downward below the uterine arteries. The clamp should not be removed until the suturing is complete. On taking it off the uterus flushes up like a limb after the removal of a tourniquet, but the flushing is temporary and subsides in a few minutes.

As regards the incision in the uterus this should be anterior and central whenever possible. Tumors lying off the middle line can be reached by secondary incisions starting from the primary incision and tunneling outward. Tumors lying in the posterior wall if not too large are to be removed "transeavily," the lumen of the uterus being opened from the front and the posterior wall being incised through the posterior endometrium.

There is no risk in opening the uterine cavity, and it has the advantage of preventing small submucous fibroids or mucous polyps being overlooked, while palpation

of the uterine wall for seedlings is best carried out with one finger in the cavity. Every fibroid down to the smallest seedling must be removed.

After the removal of a fibroid or fibroids a more or less hypertrophied uterus remains. Involution occurs as after labor but with less vigor, and the sutured organ when returned to the abdomen should not greatly exceed the normal in bulk. It is therefore necessary in most cases to cut away part of the redundant uterine wall before suturing it.

A large fibroid growing in the posterior uterine wall should be dealt with by what I call the "Hood Operation." A transverse incision is made extending from just behind the tubouterine junction on one side to a corresponding point on the other side. The incision should open the capsule of the tumor and through it the tumor should be extracted by morcellation, so as to avoid extending the primary incision by tearing it outward. The morcellation being completed a "hood" composed of the posterior uterine wall superficial to the tumor is left behind. This if too thick and stiff must be first "planed down" by the scalpel and then brought over the fundus by a series of buried sutures until the final suture line lies in a horseshoe curve on the front of the uterus with the lowest placed suture just above the bottom of the uterovesical growth.

This is a satisfactory operation to perform and leaves a perfectly smooth and normal posterior uterine wall opposed to the intestines, whereas if the fibroid is removed via an incision through the posterior wall, a suture line is left directly inviting intestinal adhesion.

There are some cases in which the number of the fibroids to be removed is too great to allow of either of the two former methods being applied. In such I perform what I call "block excision." The uterus is first bisected down nearly to the internal os. The index finger is now inserted into each cornu in turn to mark their positions, and these being defined a wedge-shaped excision is carried out on each side with its base at the fundus and its apex below. In cutting the wedge the scalpel goes through any fibroid that may be in the line of the incision. It is necessary to be certain that the cornu is not cut away in doing this, and it is for this reason that the uterus is first bisected and the positions of the cornua defined by the finger tip.

The two much reduced halves of the uterus contain fibroids that have escaped the block excision. These are enucleated and the two halves are sutured together so that the strips of endometrium on either side reconstitute the uterine cavity with its cornual extensions. This operation has the drawback of leaving a suture line on the back of the uterus.

There is another class of case to which the ordinary technic of myomeetomy is unsuited, namely, cases of cervical fibroids. The myomeetomy clamp cannot be applied in these cases until the tumor is enucleated, but the circulation through the ovario-pelvic ligaments should be controlled. The uterus is then bisected until the capsule of the tumor is opened and the tumor is then enucleated. An immensely redundant supravaginal cervix remains. This can be reduced in circumference by cutting away sufficient of the cervical wall. Before starting to do this a long narrow pressure forceps or strong probe should be pushed down the cervical canal to indicate its position, otherwise it is in danger of being cut away. The halves of the body of the uterus and the cervix are now sutured together leaving a very long cervix with the body perched up on the top of it. This condition should be dealt with by performing the Baldy-Webster operation which acutely anteflexes the uterus and the upper part of the cervix. As involution proceeds the length of the cervix will attain the normal.

Finally, as regards the suture of the enucleation cavities: a very reliable and strong catgut should be used and mattress sutures should be avoided because they tend to obstruct the blood supply. For inserting the sutures the pattern of

Reverdin's needle that I use is superior to ordinary needles because its great strength allows its being passed round cavities without fear of breakage.

It has been suggested that the uterine vessels may be damaged by the myomectomy clamp with consequent risk of embolism. It is not so; no damage is done to them. Of the seven deaths I record, two were due to pulmonary embolism, but these occurred among my early cases, before I began to use the myomectomy clamp.

## 7. When Is Surgery Indicated in Retrodisplacement of the Uterus?

Dr. George H. Gardner, Chicago, Ill. (For original article, see page 596, October issue.)

### DISCUSSION

DR. GERALD C. MELHADO, MONTREAL, CANADA (by invitation).—In considering "backward displacements" of the uterus, it is necessary to bear in mind that the uterus is essentially a specialized part of the pelvic floor, and that, within the limits of the normal position, it is permitted a wide range of movement.

The term "backward displacement" of the uterus has come to include not only variations in the position of the uterus, but also in the direction of its axis, and even of its component parts.

I believe that there is a great difference between mobile and fixed retroversion. In Dr. Gardner's series of 145 cases, he classifies 83 as essential retrodisplacements, only 9 of which were unassociated with any pathologic lesion in the pelvis. Of the 62 incidental cases, all were associated with some complicating pelvic disease. It may therefore be justifiably claimed that the associated lesions were the predominant cause of symptoms and the underlying factor for surgical intervention, the retrodisplacement playing only a minor part if any. Whether retrodisplacement may be said to be the cause of the associated lesions is, however, another story.

In the Gynecologic Department of McGill University it was taught that the normal position of the uterus was in the principal axis of the pelvis, with the cervix at the level of the ischial spines, and the fundus slightly forward of the pelvic axis; i.e., slightly anteverted and anteflexed, but that in 25 per cent of healthy women the uterus was retroverted, and that this position caused no symptoms and required no treatment.

It is undeniable that the retroverted uterus is placed at a disadvantage in the pelvis, and is subject to the intestinal and intraabdominal pressure acting directly on the uterus, and, so, is a predisposing cause of a prolapse; in fact, *it is the* first stage of a prolapse. It is in this prolapse that the importance of the condition lies, for it is this prolapse and not the retroversion which gives rise to the symptoms.

In the matter of symptoms and signs, it may be fairly said that their presence is in no sense a characteristic of retroversion, or any other displacement, and so the displacement may be but a coincidence, and possess no etiologic factor whatever.

The ovaries in retroversion, however, are specially liable to prolapse, and so exert a downward traction upon their special attachments. They then may become edematous, hypertrophic, or undergo degenerative changes and add their weight to the uterus. They may sink down into the pouch of Douglas and underlie the uterus. A tuboovarian varicocele, especially marked in the pampiniform plexus, may occur. We have had several such cases.

After a careful review of 261 cases of retroversion, occurring in the Royal Victoria Hospital during the past five years, and searching for the cause of symptoms, I was unable to conclude that the retroversion *per se* would account for them, and was forced to attribute them to a variety of associated lesions.

Again, menstrual disturbances have not been observed as being present where the uterus was maintained at its proper level in the pelvis. It has been noted, however, that, although retroversion of the uterus cannot be said to be *the* underlying factor

in causing sterility, nevertheless pregnancy has rapidly followed the simple procedure of lifting forward the body of the uterus and so making it possible for the cervix to lie in the seminal lake.

When general treatment fails and the retroversion is associated with some prolapse, a suspension operation is possibly justifiable as part of the corrective measure. The method most frequently used in the Royal Victoria Hospital is the Olshausen suspension, closing off the lateral apertures by stitching the round ligament to the anterior abdominal wall, thus preventing a possible hernia of the small bowel.

DR. HAROLD O. JONES, CHICAGO, ILL.—Our experience is parallel to that of Dr. Gardner in that the majority of patients in our clinic have been operated upon for the complication rather than for the retrodisplacement per se.

Those patients who have had defundation of the uterus have also had complications. Our greatest number were in those cases done abdominally; in our experience we had considerably fewer in those done by the vaginal route.

Our technical procedure has also paralleled that of Dr. Gardner. We follow his technic in detail. In years gone by I personally had the privilege of delivering twelve patients who had this type of operation and there was no great delay in delivery. In the patients examined subsequently there was no return of the retrodisplacement.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—In one of the group of patients just referred to upon whom I operated, death resulted from pulmonary embolus. The patient was a young woman with marked varicosities of the broad ligament veins. There were present in the operating room some six or eight guests and I am always disposed to demonstrate all of the pathology present. I lifted the uterus a distance of 8 or 9 inches to show its marked mobility, and turned it from side to side perhaps as many as four or five different times. The patient's recovery was uneventful until about the tenth day, when she had a most excruciating backache. This happened during the night and I appreciated the possibility of there being a thrombosis. She seemed well the next morning, then died suddenly with typical embolic symptoms. Since that time, I have preached to our students and associates that it behooves us to be painstakingly careful in manipulating an unduly mobile uterus, especially in the presence of dilated pelvic veins.

DR. JOSEPH L. BAER, CHICAGO, ILL.—I would call attention to the work of Sturmdorf on causes of retrodisplacement, such as differences in pelvic inclination and the effect of intraabdominal pressure on the uterus in early infancy. I think it may be accepted that in the patient in whom there is little pelvic inclination and in whom the top of the symphysis and the promontory are almost on a parallel, that that patient is going to have a retrodisplacement in adult life which in her is a part of her normal state. However, she is most likely to have the disorders that may follow in the subsequent course of the retrodisplacement.

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—In addition to a considerably larger number done earlier, I have recently seen five women operated upon by the technic which has been described, four of whom have passed through pregnancy and labor, one of them for the second time. The fifth is now pregnant. In all of these the uterus has remained in the position at which it was left at the time of operation.

Dr. Gardner spoke of the effect of retrodisplacement as a cause of sterility. I feel that retrodisplacement may be an occasional cause of sterility, but I think it is not a very frequent one because I see each year a number of women who have retrodisplacement and who are pregnant. Some of these have been pregnant a number of times. In an analysis made several years ago of 1,000 private cases to determine the incidence of retrodisplacement in pregnancy and the puerperium, we found a little over 18 per cent of retrodisplacements.

*(To be continued in the December issue.)*

## NEW YORK OBSTETRICAL SOCIETY

*MEETING OF FEBRUARY 12, 1935*

The following paper was presented:

**The Treatment of Vesicovaginal Fistulas: Past and Present.** Dr. Norman F. Miller. (By invitation. For original article, see page 675.)

*MEETING OF MARCH 12, 1935*

The following papers and case reports were presented:

**Primary Carcinoma of the Fallopian Tube.** Dr. W. T. Dannreuther. (For original article see page 724.)

**Histologic and Hormonal Studies in Chronic Mastitis.** Dr. Howard C. Taylor, Jr.

**The Histogenesis of Some Ovarian Tumors and Their Biologic Effect.** Dr. S. H. Geist. (For original article, see page 650.)

---

## OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF MAY 2, 1935*

The following paper and case report were presented:

**Hematometra.** Dr. John A. McGlinn and W. Benson Harer. (For original article, see page 704.)

**Chorionepithelioma Following Full-Term Pregnancy.** Dr. Clifford B. Lull. (For original article, see page 730.)

---

## CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF MAY 17, 1935*

The following papers were presented:

**The Toxemias of Late Pregnancy.** Drs. W. A. Thomas, E. D. Allen, C.P. Bauer, and M. R. Freeland. (For original article, see page 665.)

**Out-Patient Obstetrics.** Dr. Henry Buxbaum. (This paper will appear in the December issue.)

**Brenner Tumor of the Ovary.** Dr. Philip H. Smith. (For original article, see page 734.)

**Tubal Reimplantation—In Retrospect.** Dr. George de Tarnowsky. (For original article, see page 696.)

**Monoamniotic Twins, One Normal, the Other Anencephalic; Multiple True Knots in the Cords.** Drs. Sol Litt and Herman A. Strauss. (For original article, see page 728.)

---

## BROOKLYN GYNECOLOGICAL SOCIETY

*MEETING OF APRIL 5, 1935*

The following case report and paper were presented:

**Spontaneous Evolution of a Transverse Presentation.** Dr. William G. Fraser (by invitation). (For original article, see page 732.)

**Some New Aspects of the Menstrual Problem.** Dr. Carl G. Hartmann (by invitation).



# Department of Book Reviews

---

CONDUCTED BY ROBERT T. FRANK

---

## Review of New Books

---

### Gynecology and Obstetrics

The progress in gynecology which has taken place during the twelve years since the first edition of Dr. Anspach's book, *Gynecology*,<sup>1</sup> was published, has required numerous additions, corrections and modifications of the subject matter in the subsequent editions called for by the popularity of this work. The fifth edition has now been entirely rewritten and appears as a new book. The additions apply particularly to the sections dealing with physiology, disturbances of function, radiation treatment, endometriosis, and several others. The assistance of a number of collaborators, specialists in their various fields are acknowledged and the present edition, as have the others, affords an up-to-date knowledge of this important branch of medicine.

—George W. Kosmak

The difficulty in preparing a text suitable at once in elementary principles for the student, in presentation of symptomatology, diagnosis, and treatment for the general practitioner, and in offering surgical methods tried by years of experience and judgment for the operator has been overcome in Curtis' *Textbook of Gynecology*.<sup>2</sup> In this second edition marked by an absence of debate, a conciseness of diction, a fullness of detail where necessary, and an abundance of beautifully executed illustrations portraying carefully selected operative maneuvers, one finds a well-balanced exposition of present-day American gynecologic teaching which may be heartily recommended.

—Philip F. Williams

In this second edition of *Practical Surgery of the Abdominal and Pelvic Regions*,<sup>3</sup> Dr. Kennedy brings out the constructive principles underlying the surgical teachings of his late chief, Dr. Joseph Price. Departing from time-honored custom the author follows no rule as to order of subject matter nor of arrangement as to the pathologic lesion treated but considers all phases of pelvic disease under the operation by which they may be, in his opinion, best handled.

---

<sup>1</sup>*Gynecology*. By Brooke M. Anspach, M.D. Fifth Edition. Re-illustrated and completely revised by the author with the assistance of Philip F. Williams, M.D. and Lewis C. Scheffey, M.D. J. B. Lippincott Company, Philadelphia, Pa., 1934.

<sup>2</sup>*Textbook of Gynecology*. By Arthur Hale Curtis, Professor and Head of Department of Obstetrics and Gynecology, Northwestern University Medical School, etc. Second edition, with 300 illustrations, and 493 pages. W. B. Saunders Company, Philadelphia, 1934.

<sup>3</sup>*Practical Surgery of the Abdominal and Pelvic Regions*. By James William Kennedy, Surgeon-in-Chief to the Joseph Price Hospital, etc. Second edition, illustrated with 133 original half-tone plates, some in color, and 861 pages. F. A. Davis Company, Philadelphia, 1934.

In the first chapter vaginal hysterectomy is described in fullest detail as to indication and technic. Dr. Kennedy states he would feel no apology needed for the appearance of this volume if he could influence a trend toward more frequent use of vaginal hysterectomy. Of particular interest among the other chapters are those discussing the handling of suppurative adnexal lesions and pelvic peritonitis; undoubtedly objection may be raised to the reasoning involved in the discussion of these subjects. The volume closes with a recollection of Dr. Price's personality and sayings.

—Philip F. Williams

Béclère prefaces this monograph on *Röntgen Treatment of Uterine Fibromas and Metropathies*<sup>1</sup> with a short and interesting history of the stages of the treatment of the fibromyomatous uterus. Gibert recounts here his experience in the L' Hopital Saint-Antoine over a period of fourteen years in the roentgen therapy of fibroids and benign uterine hemorrhage. He brings out all the points of argument advanced, by the surgically inclined, against the methods, which he naturally enough seeks to refute; and the evidence in favor of this treatment, which he supports. He lays stress, however, upon the exact indications for the selection of the method and is meticulous in discussing its limitations, and the possible complications and accidents which may arise in wrongly chosen cases. In his experience he has seen but four carcinomas, two of them cervix and two of them fundus, follow roentgen treatment of the two conditions named.

In the statistical review of 350 cases, 310 followed up, five failures were due to submucous fibroids. These were cured by surgical intervention. Three ovarian cysts treated by error in diagnosis were later cured by surgery.

Gibert concludes that roentgen therapy, properly used, is superior to both radium and surgery in the treatment of myomas and benign uterine bleeding.

—Philip F. Williams

The warm reception accorded two previous monographs, "Indication" and "Diagnosis," has prompted Benthin to prepare a third book on *Treatment in Gynecology*.<sup>2</sup> The author feels that in regard to completeness of presentation and economy, in comparison to the cost of the expensive systems, much can be gained for the profession by this manner of presenting the various phases of gynecology.

In addition to discussing the treatment of the diseases and functional and organic alterations of the pelvic organs there are included chapters relating to the breast, the abdominal wall, the intestine and urinary tract, and contraceptive methods. Minor gynecologic surgical methods receive attention as to indications and usefulness. The subject of heat and other physical agents is briefly discussed. In regard to gynecologic manifestations of endocrine diseases, Benthin thinks that no outstanding results have been obtained by biologic therapy and feels that many apparent successes are due as much to general therapy as to the hormone used.

This monograph is comprehensive as to topics covered and well detailed as to ambulatory treatment and methods.

—Philip F. Williams

<sup>1</sup>In Roentgentherapie des Fibromyomes de l'uterus, et de metropathies hémorragiques. Par Paul Gibert. Avec 10 figures dans le texte, et 110 pages. Masson et Cie. Editeurs. Paris, 1935.

<sup>2</sup>Therapie der Frauenkrankheiten. Von Professor Dr. W. Benthin. Koenigsberg i. P. Mit 23 Abbildungen im Text. Verlag von Urban und Schwarzenberg, Berlin und Wien, 1934.

This book designed primarily for the general practitioner is a guide to the *Treatment of Common Female Ailments*<sup>6</sup> and has been very well brought up to date in this edition. There have been added ten new chapters including examination, the endocrine glands, menopause, perineal injuries, gastrointestinal ailments, fertility, sterility, and especially two chapters on the Prevention of Female Ailments.

The brevity of some of the material is more than made up for in the succinctness and the common sense discussion of the subjects. While emphasis has been laid upon symptoms and diagnosis, the value of the book to the practitioner is increased through the detailed discussion of treatment of minor conditions which may be handled in office practice, as well as suggestive prescriptions.

The author does not advocate glandular therapy in endocrine disturbances, although he gives an excellent review of the present status of the principles involved. The chapters on postoperative care, postnatal treatment and prevention of female ailments contain some very fine ideas on gynecologic prophylaxis. The book is highly recommended to the general practitioner.

—Philip F. Williams

The large number of individual studies of biochemic changes in the course of the various phases of reproduction call for just such a comprehensive and critical review as is offered in this small monograph entitled *Physiologic Chemistry at Birth*.<sup>7</sup> Adding to already available information the results of his own extensive investigations, the author arrives at the interesting conclusion that the process of birth in regard to chemical and physicochemical changes does not represent a unity but must be divided into four parts: Dilatation of cervix; main part of expulsion stage; actual expulsion of child, and postpartum period. The characteristics of biochemic alterations for each of these four stages are described in detail. This monograph will be of outstanding value particularly to scientific workers in this special field.

—Hugo Ehrenfest

This book reflects the heightened interest of recent years in *Obstetrical Analgesia and Anesthesia*.<sup>8</sup> The author through her hospital affiliations and experience is well qualified to write authoritatively on the subject.

The methods applicable to the various stages of labor, abnormal deliveries and complicated labors are described in detail as to choice, action, and dosage of the agents and technic. There is a timely and important section upon resuscitation of the newborn where asphyxia has resulted from the drugs administered. The applicability of the various methods of analgesia and anesthesia to house practice is fully discussed.

That the dosage of some drugs has been calculated upon the English system of weights, stones, and pounds, does not lend the tables to universal use. The adoption of a parallel metric system might have been in order. Many American obstetricians question the suggested use of morphine shortly before delivery, others do not favor the recommended wide use of spinal anesthesia in cesarean section,

<sup>6</sup>*Treatment of Common Female Ailments*. By Frederick John McCann, Consulting Surgeon, Samaritan Free Hospital for Women, London, etc. Third edition. 370 pages. William Wood & Co., Baltimore, 1934.

<sup>7</sup>*Die Physiologische Chemie der Geburt*. Von Dr. Heinz Sledentopf, Privatdozent fuer Geburtshilfe und Gynaekologie an der Universitaet Leipzig. Pp. 130. Mit 5 Kurven und 21 Tabellen. Johann Ambrosius Barth, Leipzig, 1932.

<sup>8</sup>*Anaesthesia and Analgesia in Labour*. By Katharine G. Lloyd-Williams, M.D., Honorary Anaesthetist to the Royal Free Hospital in London, etc. With foreword by Dame Louise Mellroy, Professor of Obstetrics and Gynaecology, London School of Medicine for Women. 96 pages. William Wood & Co., Baltimore, 1934.

while others would regard the omission of mention of local anesthesia in the section dealing with toxemias a serious fault in the presentation of the subject.

Otherwise there is very much worth while in this full, though concise, analysis of the various methods of analgesia and anesthesia.

—Philip F. Williams

### Miscellaneous

The author of *Economic Problems of Medicine*<sup>9</sup> was a signer of the minority report of the Committee on the Costs of Medical Care. He subjects the social and economic problems of medicine to a critical analysis in a series of topical discussions and brings out strongly the rights of the physician in the presently changing methods of practice.

His ideas regarding the socialistic merger of Medicine with a machine-age type of practice will be shared by all intelligent physicians. He presents some remarkable figures regarding the extent of present hospital facilities and indicates a reduction of their cost. The obligation of the physician to the medical organizations stresses the effect of collective action in many health problems. The relation of the physician to the community should be to preserve the personal relation of physician and patient. The author vigorously upholds the recommendations of the minority group who discussed the medical care of the American people.

There is a careful analysis of the various present and proposed systems and schemes of compensation and health insurance, foreign and domestic, and the subject of industrial medicine is fully covered. The newer methods of medical and dental care as worked out locally in various areas are dissected and discussed. The author indicates that no one plan may be feasible in all districts. He describes the possible developments which may ensure health to the nation and position and progress for the medical profession. The book should be widely read.

—Philip F. Williams

A Committee of the Western Surgical Association has compiled a list of the *Names of Surgical Operations*.<sup>10</sup> This nomenclature greatly reduces the multiplicity of names of surgical operations and has dropped the eponymic terminology in favor of a common sense anatomic term describing the procedure employed. The classification provides not only for uniformity, but allows for a flexibility found in an advancing science, and a continuity of the system may be provided by periodic revisions.

The names of operations are listed by system. At the foot of each page is a set of qualifying words and phrases which may be added to the names of surgical operations. There is an appendix listing fundamental surgical procedures, another discussing philologic suggestions and corrections, for some criticisms will be made by the purists, and a final appendix on commonly used suffixes.

The original number of operations listed and sent out for correction was 3,313. The number was thus reduced to the 743 titles given. This reduction of 75 per cent of the bulk of words and phrases used in the present recording of surgical procedures is praiseworthy. An example of this reduction which should be of interest to all gynecologists is given on pages eight et seq. where a list of sixteen

<sup>9</sup>*Economic Problems of Medicine*. By A. C. Christie, M.S., M.D., Professor of Clinical Radiology, Georgetown University, Medical School, etc. 242 pages. The Macmillan Company, New York, 1935.

<sup>10</sup>*Names of Surgical Operations*. Compiled and arranged by the Western Surgical Association through its Special Committee. Edited by Carl E. Black, A.M., M.D. 102 pages. Bruce Publishing Co., St. Paul, Minn., 1935.

operations, the majority of the titles eponymic, have been reduced in the present system to two operations. It is apparent that some alterations and additions should be made in the list of names of obstetric operations. In the index, one finds 103 operations listed under delivery; under uterus, 26 procedures are listed.

Such a list will be to surgical records of the future what the Basle Nomenclature is to anatomy and what the new Standard Nomenclature of Diseases is to the record filing room. This list deserves the adoption and warm support of all surgical clinics. The Editor requests corrections, criticisms, and other suggestions.

—Philip F. Williams

This book entitled *Dynamics of Population*<sup>11</sup> represents an extended inquiry into certain social and demographic data which bear upon the reproduction trends and other differentials in the various racial and cultural groups which make up our national population.

The population growth in the United States is slowing down. The authors of this study feel that an equilibrium will be reached in from twenty to forty years with a maximum population of some 150 million or less. The trends of social and genetic heritage responsible for the decrease have been analyzed, with a study of the by-effects of communal resistance or expansion, and economic status as modifying influence on the above factors. A study of the fertility and reproduction differentials in these groups leads the authors to feel there will be little probability of any levelling of or reversals of these differentials.

The measurable characteristics of American groups especially as regards health and cultural-intellectual development when studied from various available documented sources showed a constant finding of high frequency of individual ability in the upper social classes. However trite this conclusion may sound, the observations which lead to it form an intensely interesting survey of our socio-economic and occupational groups.

The final section of the book on the causes and control of population trend brings out many factors which will merit the attention of eugenists and those of the profession who may be interested in the broader aspects of fertility, sterility, and the control of reproduction. With candor and without bias the physical and medical, as well as the economic and social, factors affecting fertility are reviewed. Such remedies for the avoidance or correction of the factors resulting in unfavorable differentials in the birth rate are discussed in the final chapter on social control. One feels the broadminded attitude of the authors toward the whole subject of social control epitomized in the section "conditions affecting the economic security of young couples."

There are various appendices of supporting material, a glossary and a documentation of sources of material. To the eugenicist, the student of society, and the physicians this book will be of great interest and value. To the obstetrician it brings in another manner to our attention what Litzenberg has termed, "the challenge of the falling birth rate."

—Philip F. Williams

This volume is intended to cover the whole subject of *Birth Control*<sup>12</sup> for the general public. The author has admirably succeeded in her task. No longer a

<sup>11</sup>*Dynamics of Population*. By Frank Lorimer and Frederick Asborn. The Macmillan Company, New York, 1934.

<sup>12</sup>*Birth Control, Its Use and Misuse*. By Dorothy Dunbar Bromley, with an Introduction by Dr. Robert Latou Dickinson. 301 pages. Harper & Brothers, New York, 1934.

controversial topic but a living issue forced upon us by economic circumstances it is timely that such a complete and sanely written discussion for the laity on control of births has appeared.

The various methods of contraception, ancient and modern, natural and mechanical are described. The fallacy of the low risk period of the Ogino-Knauss theory is exploded. The reluctant attitude of organized medicine to have the archaic Comstockian Federal and State laws revised is fittingly chided. The illegal abortion problem in this country and the legal abortion problem in the Soviet area are well handled. The author's references show very certainly that legalized abortion is no solution to the problem of birth control. There is a chapter on sterilization and one on sterility which are quite in place in a book of this nature. A very extensive recent bibliography and a résumé of the State laws on contraception complete the book.

—Philip F. Williams

The jacket of this book<sup>12</sup> contains the statement that due to existing laws regarding the dissemination of *information upon birth control* this volume is to be sold only to physicians or upon a physician's prescription. This is rather an anomaly when one realizes the enormous amount of thinly veiled literature distributed openly upon feminine hygiene in the United States today.

In this small volume Fielding discusses the methods he has found of most value in his work in England. He makes a very good case for birth control in his clear chapters on the sociologic factors and meaning of the movement to free this branch of medicine from its present legal shackles. He ably refutes many of the objections to an open knowledge of the subject by the public and the instruction of the laity by physicians on birth control methods.

—Philip F. Williams

In a remarkable series of sixty-four photographic studies, Killian has portrayed the *Facial Expressions of Pain*<sup>13</sup> observed in a large variety of diseases. Technically the work was accomplished in natural light with a Rolliflex camera, yellow filter, and superpan film. The result of his labors is an outstanding contribution to photography in clinical medicine. The changes shown in the face during the progress of a case of juvenile sarcoma, and of a case of tuberculous peritonitis are more striking evidence of the advance of the disease than any progress notes could ever be.

Killian pleads for a more extended use of the camera in recording the ravages of the disease not only upon the physical make-up of the face but also upon its superphysical or spiritual embodiment. He feels that in this way physicians may be trained to a greater degree in the art of observation of emotional and psychical manifestations of disease as contrasted with the somatic alterations of the countenance.

—Philip F. Williams

The thin paper and small type used has permitted a great deal more material to be included in this small book on *Genitourinary Diseases*<sup>14</sup> than its size would indicate. In the first four chapters the text offers the essential principles govern-

<sup>12</sup>"Parenthood. Design or Accident? A Manual of Birth-Control. By Michael Fielding, M.D. With 8 illustrations, and 239 pages. The Vanguard Press, New York, 1935.

<sup>13</sup>"Facies Dolorosa. Das Schmerzliche Antlitz. Von Dr. H. Killian. Mit 64 Abbildungen. 88 pages. Verlag von Georg Thieme, Leipzig, 1934.

<sup>14</sup>"Synopsis of Genitourinary Diseases. By Austin I. Dobson, Professor of Genitourinary Surgery, Medical College of Virginia. With 111 illustrations. The C. V. Mosby Co., St. Louis, 1934.

ing diagnosis, examination, anatomy, and anomalies. Following this the separate diseases and conditions of the urologic tract are considered seriatim. While lacking the full detail of a larger text, the book offers a sufficient discussion as to diagnosis and treatment to be of much value to the physician in general practice.

—Philip F. Williams

The author presents this book as the result of his researches into the manifestations of the relation of *rheumatism and disorders of the autonomic nervous systems*<sup>16</sup> to various organic and systemic diseases.

In considering the female reproductive system in regard to this relationship he discusses two types of dysmenorrhea, the hypertensive and the hypotensive. The former he feels is due to a hyperaugmentation of the uterine os through the thoracolumbar system, the latter is due to a contraction of the body of the uterus. The stimulating causes are mental, toxic, and allergic. Menorrhagia he regards as due to an imbalance of the autonomic system. This may appear through either excessive inhibiting action or through deficient augmentatory action of both systems. In pregnancy the hypertonic, excessive augmentative action of the thoracolumbar system, causes slow dilatation of the cervix, and a tendency to toxemia; the opposing or opposite system predisposes toward relaxation, easy labors and hemorrhage from a lack of pressor influences.

Whether all the author's theories in regard to arthritis and other joint conditions will be accepted remains to be seen.

—Philip F. Williams

---

<sup>16</sup>The Autonomic Diseases or Rheumatic Syndrome. By Dr. T. M. Rivers. 209 pages. Dorrance & Company, Inc., Philadelphia, 1934.

# Items

## ANNOUNCEMENT

During the Spring of 1935 a committee for the study of sex variants was formed with the following membership: Chairman, Eugene Kahn, M.D., Yale University; Secretary, Robert W. Laidlaw, M.D., Columbia University; Treasurer, Carney Landis, Ph.D., Columbia University. These three officers, together with Robert L. Dickinson, M.D., National Committee on Maternal Health, and Josephine H. Kenyon, M.D., Columbia University, constitute the Executive Committee. The Committee members are Clarence O. Cheney, M.D., Columbia University; Maurice R. Davie, Ph.D., Yale University; Earl T. Engle, Ph.D., Columbia University; George W. Henry, M.D., Cornell University; E. A. Hooton, Ph.D., Harvard University; Marion E. Kenworthy, M.D., New York School of Social Research; K. S. Lashley, Ph.D., Harvard University; Adolf Meyer, M.D., Johns Hopkins University; Catharine Cox Miles, Ph.D., Yale University; Harold D. Palmer, M.D., University of Pennsylvania; Philip E. Smith, Ph.D., Columbia University; Edward A. Strecker, M.D., University of Pennsylvania; Lewis M. Terman, Ph.D., Stanford University; and Dorothy S. Thomas, Ph.D., Yale University.

The objects and reasons for the organization of this Committee are the following:

1. To correlate the various scientific interests in this field of study.
2. To serve as a scientific sponsoring agency for the furtherance of research on sexual variation.
3. To appoint advisory sub-committees for projects sponsored or to be sponsored by the Committee.

At the present time the Committee is sponsoring several projects dealing with homosexuality as it appears in various classes of society. A study of 50 male and 50 female homosexuals of cultured background is already under way. Plans are far advanced for: (1) A study of homosexuality as it exists among members of the U. S. Marine Corps; and (2) A study of homosexual practices among adolescent boys who are inmates of an institution for juvenile delinquency. These projects include a psychiatric, endocrinological, roentgenological and hormonal approach to the problem.

The Committee will be glad to consider any research projects which may be presented that have a bearing upon the physiological, psychological, psychiatric or sociological problems of sex variants, and to act in a sponsoring and advisory capacity should such projects be approved.

All communications should be addressed to the Secretary, Dr. R. M. Laidlaw, at 199 Fort Washington Avenue, New York City.

---

## American Board of Obstetrics and Gynecology Examination

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, December 7, 1935.

Application blanks and booklet of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for this examination must be filed in this office not later than November 1, 1935.



## American Association of Obstetricians, Gynecologists and Abdominal Surgeons

At the last Annual Meeting of the Association, held September 16, 17, and 18, of the current year, the following officers were elected:

Dr. Louis E. Phaneuf, President  
Dr. James W. Kennedy, President-elect  
Dr. F. H. Falls, Vice President  
Dr. Lewis F. Smead, Treasurer  
Dr. James R. Bloss, Secretary  
Dr. Leroy A. Calkins, Assistant Secretary  
Dr. W. T. Dannreuther and Dr. M. Pierce Rucker,  
members of the Executive Council.

---

## The Central Association of Obstetricians and Gynecologists

The Seventh Annual Meeting of the Central Association of Obstetricians and Gynecologists was held in Omaha, October 10, 11, and 12. The guest speaker was Dr. Walter T. Dannreuther of New York. The following officers were elected:

President, Dr. Buford G. Hamilton, Kansas City, Mo.  
President-elect, Dr. Jeane Paul Pratt, Detroit, Mich.  
Vice President, Dr. James R. Garber, Birmingham, Ala.  
Secretary-Treasurer, Dr. Ralph A. Reis, Chicago, Ill.

Detroit was chosen as the meeting place for 1936.

---

## Errata

In Dr. Samuel H. Geist's article in the October issue of the JOURNAL on page 483, the legend for Fig. 4 should read "Lipoid stain showing presence of fat globules in the tumor cells." Also on page 490, the legend for Fig. 14 should read "Showing connective tissue arrangement with fine fibrils extending into the cellular islands and surrounding the individual cells."

---

The author of an article entitled: Maternal Morbidity and Mortality in the Philippine General Hospital, abstracted in our JOURNAL 29: 239, 1935, is Dr. H. Acosta-Sison.

---

On page 447 of the September issue of the JOURNAL in footnote 19 the title of the book should read "Healthy Babies Are Happy Babies".

## Books Received

---

**THE STORY OF MEDICINE IN THE MIDDLE AGES.** By David Riesman, M.D., Sc.D., Professor of History of Medicine and Professor Emeritus of Clinical Medicine, University of Pennsylvania, etc. Illustrated. 402 pages. Paul B. Hoeber, Inc., New York, 1935.

**THEORY AND PRACTICE OF ANESTHESIA.** By M. D. Nosworthy, M.D., Anaesthetist to Westminster Hospital, Grosvenor Hospital for Women, etc. With 35 illustrations, 224 pages. Hutchinson's Scientific Publications, London, E.C.4., 1935.

**GYNECOLOGICAL AND OBSTETRICAL TUBERCULOSIS.** By Edwin M. Jameson, M.D., Fellow of Trudeau Foundation, Attending Surgeon, Saranac Lake General Hospital, etc. Illustrated with 31 engravings, 256 pages. Lea & Febiger, Philadelphia, 1935.

**MEN AND WOMEN.** *The World Journey of a Sexologist.* By Magnus Hirschfeld. English version, illustrated, 325 pages. G. P. Putnam's Sons, New York, 1935.

**YOUR NEW BABY.** *How to Prepare for It, How to Care for It.* By Linda McClure Woods, R.N. Illustrated. Robert M. McBride & Co., New York, 1935.

**MIDWIFERY.** By Ten Teachers. Under the direction of Clifford White, M.D., F.R.C.P.(Lond.), F.R.C.S.(Eng.), etc. Edited by Sir Comyns Berkeley, J. S. Fairbairn and Clifford White. Fifth edition, illustrated, 740 pages. William Wood & Co., 1935.

**ETUDOS CIRURGICOS.** Par Eurico Branco Ribeiro. I. Serie. Pp. 241. Sociedade Editora Medica Limitada. São Paulo, Brasil, 1934.

**PUERPERAL GYNECOLOGY.** By J. L. Babis, M.D., F.A.C.S., Consultant in Obstetrics, Gynecologist, Mt. Sinai Hospital, Cleveland, Ohio, etc. Illustrated, 199 pages. William Wood & Co., Baltimore, 1935.

**PRINCIPLES AND PRACTICE OF MEDICINE.** Originally written by the late Sir William Osler. Twelfth edition; revision made by Thomas McCrae, Professor of Medicine, Jefferson Medical College, Philadelphia. 1196 pages. D. Appleton-Century Co., New York, 1935.

**PREVENTIVE MEDICINE AND HYGIENE.** By Milton J. Rosenau, Professor of Preventive Medicine and Hygiene, Harvard Medical School. Sixth edition. D. Appleton-Century Company, New York, 1935.

**LIFE BEGINS.** *Childbirth in Lore and in Literature.* By Morris Braude, Associate Professor of Psychiatry, Rush Medical College, University of Chicago. 163 pages. Argus Books, Chicago.

**OBSTETRICS for the General Practitioner.** By J. P. Greenhill, Professor of Gynecology, Loyola University School of Medicine, Chicago. Edited by Morris Fishbein, M.D. 394 pages. National Medical Book Company, Inc., New York, 1935.

TRAITEMENT DE L'ECLAMPSIE. Par B. Stroganoff, Leningrad. Préface de H. Vignes. 112 pages. Masson et Cie, Paris, 1935.

THE OBSTETRIC PELVIS. By Herbert Thoms, Associate Professor of Obstetrics and Gynecology, School of Medicine, Yale University. With drawings and photographs by the author. 128 pages. Williams & Wilkins Company, Baltimore, 1935.

DISEASES OF WOMEN. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Eighth edition, entirely revised and reset. With 1058 engravings, 999 pages. The C. V. Mosby Co., St. Louis, 1935.

INFANT NUTRITION. By William McKim Marriott, Professor of Pediatrics, Washington University School of Medicine. Second edition. The C. V. Mosby Co., St. Louis, 1935.

LEHRBUCH DER GEBURTSHILFE. Herausgegeben von Professor Dr. W. Stoeckel, Geh. Medizinalrat, Direktor der Universitäts-Frauenklinik in Berlin. Vierte, verbesserte Auflage, mit 620 zum grössten Teil farbigen Abbildungen in Text. 1036 pages. Verlag von Gustav Fischer, Jena, 1935.

OBSTETRICAL PRACTICE. By Alfred C. Beck, Professor of Obstetrics and Gynecology, Long Island College of Medicine, etc. With more than one thousand illustrations, 702 pages. Williams & Wilkins Company, Baltimore, 1935.

IMMUNOLOGY. By Noble Pierce Sherwood, Ph.D., M.D., Professor of Bacteriology, University of Kansas, and Pathologist of the Lawrence Memorial Hospital, Lawrence, Kansas. Illustrated, 608 pages. The C. V. Mosby Company, St. Louis, 1935.

THE PARATHYROIDS, in Health and in Disease. By David H. Shelling, M.D., The Johns Hopkins University and Hospital, Baltimore. Illustrated, 335 pages. The C. V. Mosby Company, St. Louis, 1935.

Witherspoon, J. Thornwell: *Uterine Hemorrhage, A Simple and Practical Classification*, New Orleans M. & S. J. 87: 751, 1935.

The author offers a simple classification of common forms of irregular uterine bleeding based on the age of patients. Patients are divided into two groups: from 20 to 30, and from 40 upward. He realizes a difficulty in the intermediate group, 30 to 40 years, where the two groups overlap. In the younger group he lists (1) bleeding associated with some phase of pregnancy such as abortion and ectopic pregnancies, (2) acute pelvic infections, (3) endocrine disturbances, and (4) obstetric injuries (malpositions of the uterus, erosions, eversion, and lacerations). In the older group he lists in order of importance: (1) Cancer of the cervix and fundus, (2) hyperplasia of the endometrium, (3) submucous fibroids, (4) ovarian tumors, (5) cervical or uterine polyp.

The author emphasizes the fact that abnormal bleeding at the time of the menopause should be investigated by diagnostic curettage when the cause of the bleeding cannot be determined by other examination.

EUGENE S. AVER.

# American Journal of Obstetrics and Gynecology

---

VOL. 30

DECEMBER, 1935

No. 6

---

## Original Communications

---

### FURTHER STUDIES ON THE MECHANISM OF LABOR\*

W. E. CALDWELL, M.D., F.A.C.S., H. C. MOLOY, M.Sc., M.D.,  
AND D. ANTHONY D'ESOP, PH.B., M.D., NEW YORK, N. Y.

*(From the Department of Obstetrics and Gynecology, Columbia University and the  
Sloane Hospital for Women)*

THE investigation which was instituted by one of us (W. E. C.) at the Sloane Hospital for Women over three years ago had, as its chief objective, the anatomic elucidation of the mechanism of labor and the explanation of the more common causes of arrested labor. The form of the pelvis received first consideration, chiefly because it lends itself more readily to roentgenologic visualization than other factors concerned in labor. In two recent communications the observations were described in detail, at which time a new classification of the female pelvis was proposed.<sup>1, 2</sup> Last year in a third publication we described the use of roentgenologic methods of examination early in labor to determine the frequency of occurrence of anterior, transverse, and posterior positions of the fetal head at the inlet in relation to the pelvic type in a consecutive series of 215 primigravida women and at the same time described the common method of engagement of the fetal head.<sup>3</sup>

The principles worked out during these preliminary studies have been most helpful in the present investigation of the mechanism of

---

\*Read at the Sixtieth Annual Meeting of the American Gynecological Society held at Hot Springs, Va., May 27 to 29, 1935.

---

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

labor throughout the lower levels of the pelvis. No attempt is made to give statistical data in this paper. Instead, we are describing what to us are some of the outstanding observations in the careful study of over 1,000 complete roentgenologic examinations of the pelvis and fetal head obtained before, during, or after labor in conjunction with the known details of the actual delivery and the facts ascertained by vaginal examination.



Fig. 1.—Lateral roentgenogram early in labor. *A. B.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. Extreme posterior parietal position at inlet. Such a marked degree is rare. Note relationship of *C. D.* to *E. F.* and *A. B.*

Careful study of the lateral roentgenograms illustrated in Figs. 1 to 7, in which the fetal head and its long axis (*C. D.*), the true conjugate (*A. B.*), and a perpendicular through its midpoint (*E. F.*), as well as the pubic and sacral boundaries of the true pelvis from the lateral aspect have been outlined, will bring out several important points relating to the entire mechanism of labor. These facts are separately dealt with in greater detail later in the text.

The marked obliquity of the long axis of the fetal head to the true conjugate diameter or its perpendicular, illustrated in Figs. 1 and 2, accounts for the positions assumed by the vertex in extreme examples of a posterior and anterior parietal

position. In Figs. 3 and 4 the more usual degree of obliquity is shown. The long axis of the head, however, is still at an angle to the inlet. With engagement and descent into the true pelvis a marked change in the direction of the long axis of the head occurs, and in Figs. 5 and 6 it will be noted that *C. D.* is now directed downward and backward away from the perpendicular *E. F.* The axis of the head in Fig. 5 is directed posteriorly forming a wide angle to *E. F.*, and in Fig. 6 the head has descended to a low level with its long axis parallel and close to the sacrum. After



Fig. 2.—Lateral roentgenogram early in labor. *A. B.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. Extreme anterior parietal position, so rare in this degree as to be considered an obstetrical curiosity. Note relationship of *C. D.* to *E. F.* and *A. B.*

rotation has occurred and the vertex has descended into the lower fore pelvis (Fig. 7), the axis of descent again shows no relationship to the perpendicular of the inlet, but seems obviously parallel with the symphysis and descending rami of the pubes. It will be observed that the perpendicular to the true conjugate *E. F.* serves merely as an axis of reference from which the angular relationship of the long axis of the head within the true pelvis may be determined.

The extreme example of the posterior parietal position or the so-called Litzmann's or Varnier's obliquity, illustrated in Fig. 1, is quite rare, but the lesser degree of the same obliquity, as illustrated in Fig. 3, represents in our experience the common position at the time of engagement. As descent occurs from this or any position into the true pelvis, the long axis of the fetal head swings downward and backward, while the fetal axis is carried forward until the line of descent,

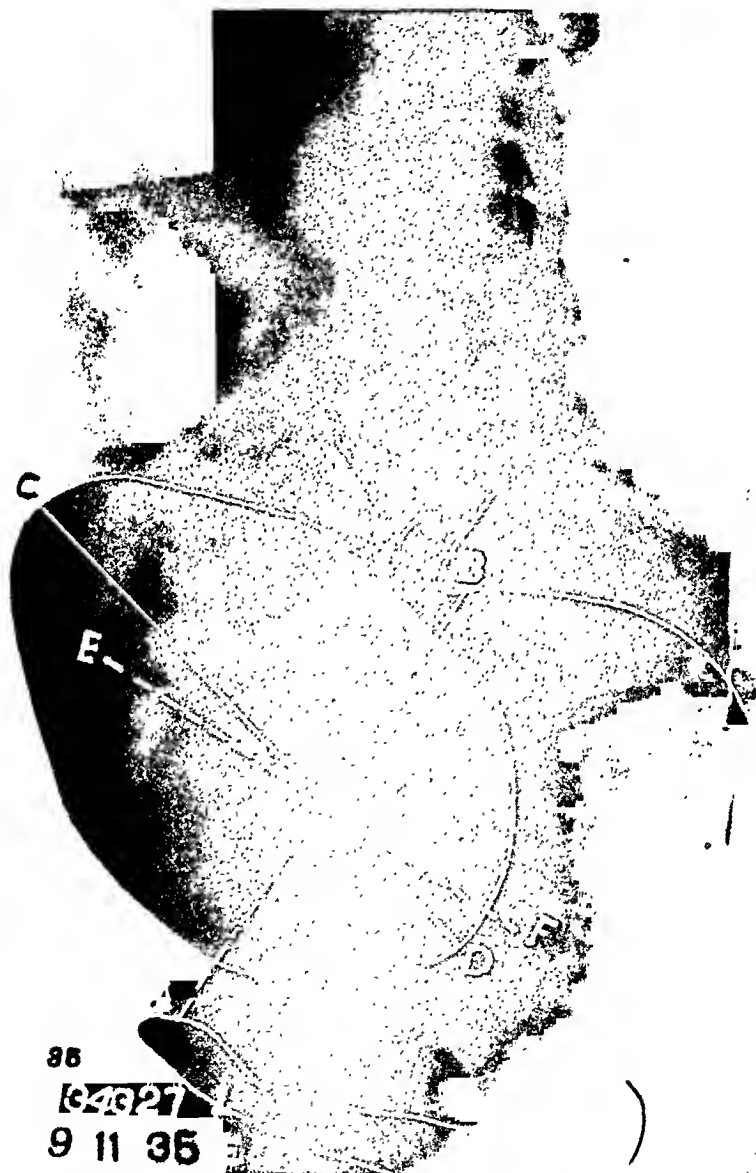


Fig. 3.—Lateral roentgenogram early in labor. *A. E.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. The usual degree of a posterior parietal position at the inlet. This degree of asynclitism is the average at engagement. Note that *C. D.* slopes forward to *E. F.* pointing into fore pelvis.

having crossed behind the perpendicular of the inlet, points toward the bottom of the posterior pelvis as represented by the anterior surface of the lower sacrum (compare Fig. 3 with Figs. 5 and 6). This curve of descent from the upper fore pelvis to the bottom of the posterior pelvis necessitates that the posterior parietal bone and sagittal suture, originally felt near the symphysis, is carried downward

and backward, becoming less easily palpable, while the anterior parietal becomes more accessible to the examining finger as the level of the midpelvis is approached. Though the head is constantly adapting itself to the pelvis, the chief factors which cause rotation become operative at this level. Synchronous with rotation, the head descends and moves forward along the inclined muscular plane of the lower fore pelvis until the back is close to and parallel with the symphysis.

The typical anterior parietal position or Nägele's obliquity, in which the sagittal suture points toward the promontory of the sacrum as in Fig. 2, in our experience is so rare as to be considered almost an obstetric curiosity. Lesser degrees of the

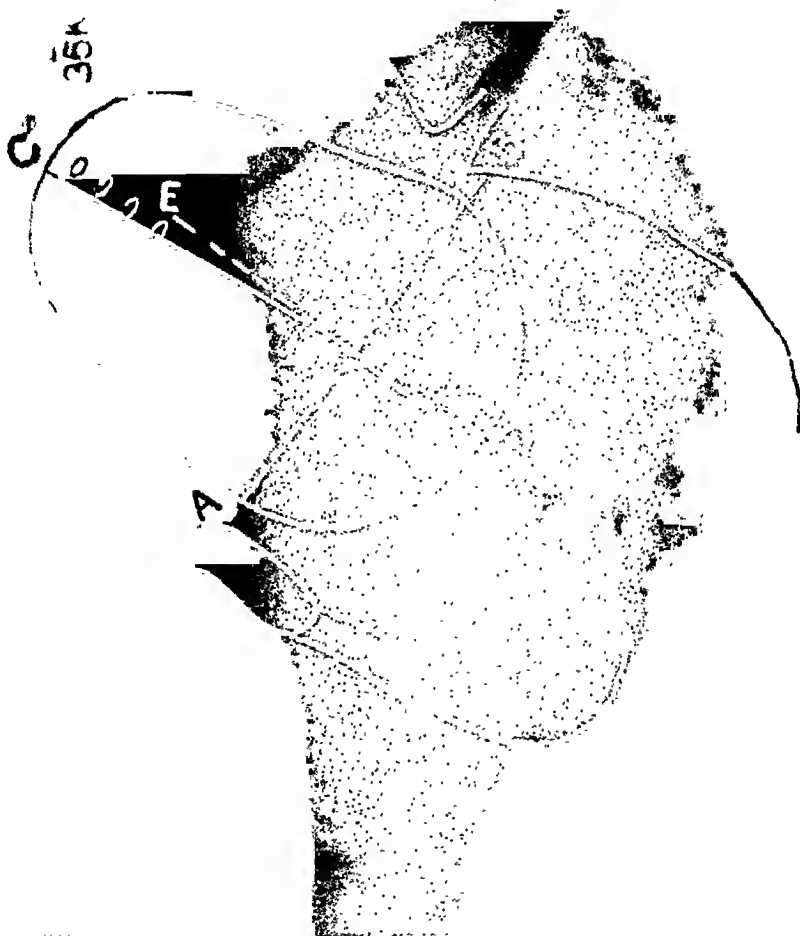


Fig. 4.—Lateral roentgenogram early in labor. *A. B.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. A relatively rare, but no uncommon form of an anterior parietal position at the inlet. Note that *C. D.* is almost perpendicular to the inlet but is inclined slightly behind *E. F.* This tendency is more noticeable when the fetal spine is located and found to be in front of the perpendicular *E. F.*

same position, as illustrated in Fig. 4, are somewhat more frequent, but when such a position is found, it is usually associated with a sagging forward of the uterus, carrying with it the body of the fetus. If the relationship of *C. D.* to *E. F.* is closely studied in Fig. 4, it will be noted that, although the head is, to all intent and purpose, perpendicular to the inlet *A. B.*, its long axis *C. D.* points slightly behind *E. F.* This minor anterior parietal tendency becomes more obvious when the long axis of the head is associated with the line of the fetal vertebral column, when it will be found that the fetal axis is definitely in front of the perpendicular of the inlet. The axis of descent, under these circumstances, is straight downward



and backward in the line of the long axis of the fetal head *C. D.* until at a low level in the posterior pelvis the head is found almost parallel to the sacrum as in Fig. 6. The principle of descent is similar for both these minor posterior and anterior parietal tendencies at the inlet. The posterior parietal tendency necessitates that the long axis of the fetal head *C. D.* cross behind the perpendicular in conjunction with a forward movement of the uterus in labor. In the case of an anterior parietal tendency, or with any head which at the onset of labor is fitting squarely in the inlet,



Fig. 5.—Lateral roentgenogram in labor. *A. B.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. Engagement has occurred. Note that the long axis of head *C. D.* is directed against sacrum behind *E. F.*, having engaged from a posterior parietal position.

the first part of this movement is unnecessary (compare Figs. 3 and 4). For both, the normal line of descent is one which carries the head downward and backward, ultimately at or behind the perpendicular of the inlet to the bottom of the posterior pelvis close to the lower aspect of the sacrum.

What factors may be suggested in explanation of this method of engagement? A study of the relationship of *E. F.* to *C. D.* in Figs. 5 and 6 will indicate that

this posterior curve of descent can scarcely be considered primarily due to the static pelvis, because in Fig. 5 the long axis of the head at that particular level is directed against the sacrum, not parallel with it as in Fig. 6. We believe that the lower pole of the uterus plays an important directing rôle in this mechanism, in conjunction with a forward movement of the uterus and the fetal axis.

Another important point which needs further explanation concerns the particular static axis followed by the head through the pelvis. The region used consistently by

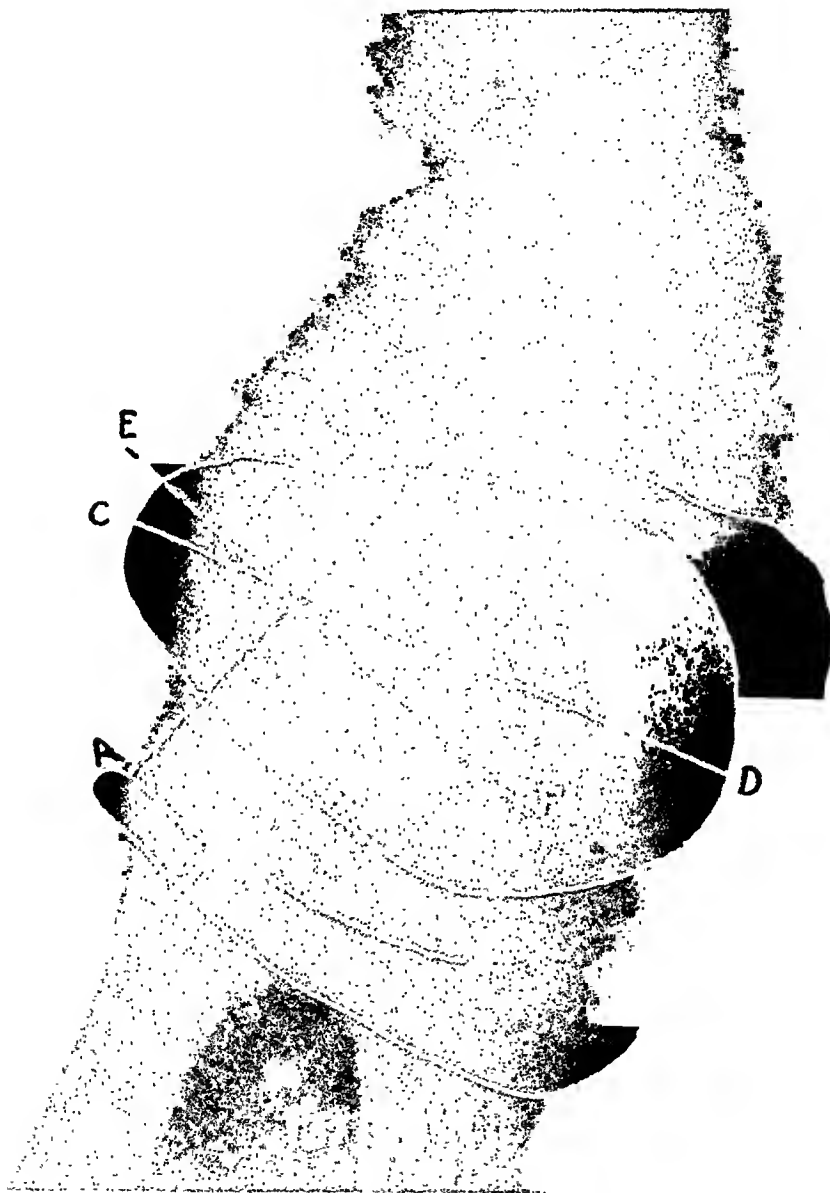


FIG. 6.—Lateral roentgenogram in labor. A. B., First plane of inlet and true conjugate diameter. C. D., Long axis of fetal head. E. F., Perpendicular to inlet through midpoint of true conjugate diameter. Engagement has occurred. Note that C. D. is parallel to sacrum and behind E. F. In this case, engagement occurred from a slight anterior parietal position as in Fig. 4.

the head in all pelvis is indicated to advantage in Fig. 55. In all pelvis, the widest transverse diameters are located behind the midpoint of the anteroposterior diameter. In order that the head may make consistent use of this more ample region, the lower pole of the uterus guides it into the posterior pelvis close to the sacrum and offers a restraint which prevents it from encroaching too soon on the fore pelvis where

narrower diameters may exist. In Fig. 55, it will be observed that the major portion of the head is located behind and above the ischial spines. The fore pelvis is avoided. Thus the central axis of the superior strait is too far forward in the pelvis to represent the axis followed by the head through the true pelvis. This latter axis of the posterior pelvis is illustrated in Fig. 24 (*C. D.*).

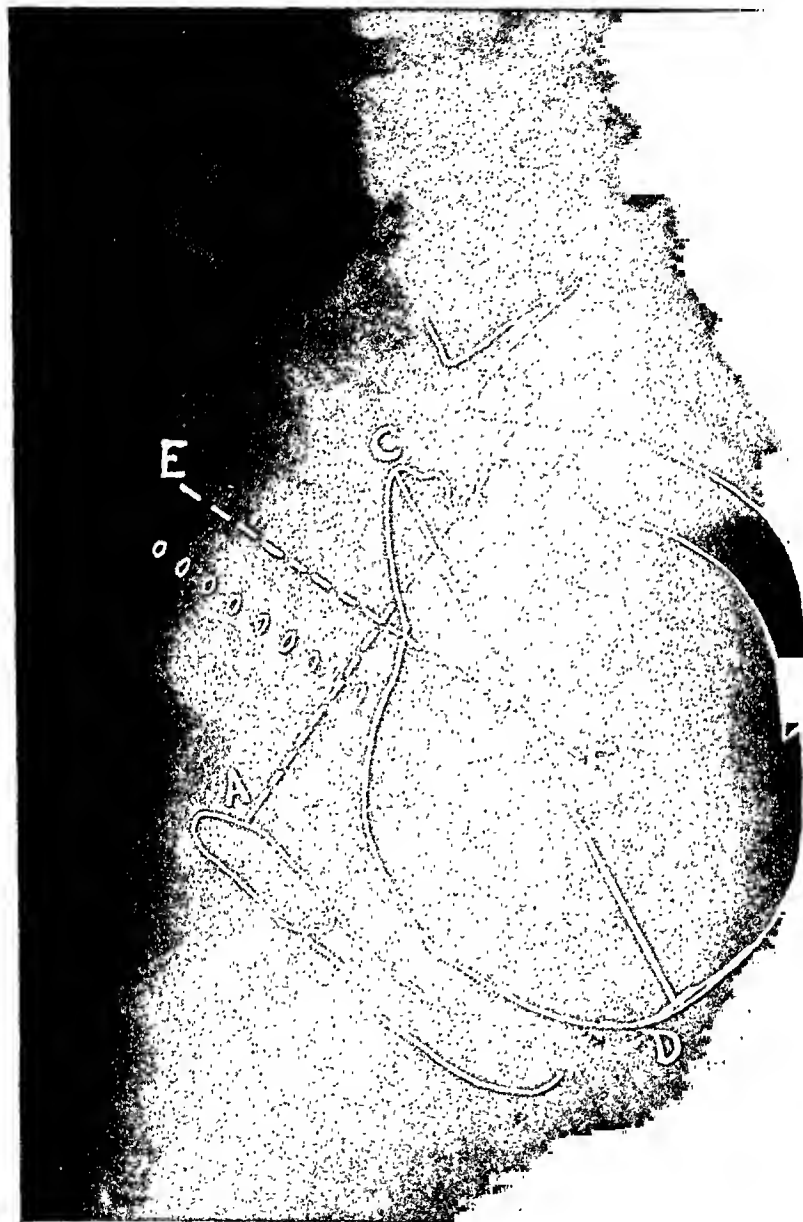


Fig. 7.—Lateral roentgenogram late in labor. *A. B.*, First plane of inlet and true conjugate diameter. *C. D.*, Long axis of fetal head. *E. F.*, Perpendicular to inlet through midpoint of true conjugate diameter. Head in fore pelvis with back anterior and parallel to symphysis. Long axis of head *C. D.* points into upper posterior pelvis. Fetal back in advance of *E. F.* in axis of fore pelvis (see *G. F.*, Fig. 24).

In these roentgenograms it will also be observed that the anterior boundary of the fore pelvis is not the width of the symphysis alone, as usually accepted, but includes the entire depth of the fore pelvis consisting of the posterior aspects of the symphysis and the pubic rami. The true pelvic cavity, therefore, actually approaches the form of a parallelogram, in which the anterior bony boundary is comparable in length to the pelvic surface of the sacrum posteriorly.

The above findings illustrated in Figs. 1 to 7, obtained by repeated stereorontgenograms and large lateral films of the pelvis during labor, have occurred so consistently in normal labor as to be interpreted by us as the usual or average method of descent. To explain fully the mechanism of labor, other factors besides those of the planes and axes of the static pelvis have to be taken into account. There is, for instance, the axis of the uterus proper and its lower pole; also the muscular and ligamentous gutter of the pelvic outlet. All of these and other points will be considered in detail under the following heads:

1. Relationship of the bony inlet to the outlet as influencing the mechanism of labor.
2. A discussion of the points of origin of the true conjugate diameter at the inlet in relation to the various planes and axes of the pelvis.
3. The axis of the uterine soft parts in the upper pelvis; the soft parts of the lower pelvis and their significance.
4. The axis of the true pelvis as revealed by this investigation, and as compared to the accepted conception of the pelvic axis.
5. The normal mechanism of labor described and illustrated, showing the application of the principles described.
6. The manner in which the abnormal pelvis may modify this normal mechanism will be limited to a discussion of the following: (a) The mechanism of labor in android (male) types. (b) Fetal pelvic adaptation at the inlet in relation to the shape of the inlet. (c) The type of pelvis associated with the persistent posterior position.

#### I. RELATION OF THE BONY INLET TO THE OUTLET

This investigation of the mechanism of labor, which virtually represents the clinical application of our previous studies on the variations in pelvic architecture, has been gratifying in two ways. It has substantiated the accuracy of the original anatomic description of each of the four parent types, the gynecoid, android, anthropoid, and platypelloid forms. And it has made it possible to observe the ease with which the shape of the pelvis may be correlated to the mechanism of labor.

The widest transverse diameter of the inlet is used to divide the inlet into an anterior and posterior segment, each of which displays a characteristic shape for the four parent pelvic types, Figs. 8 to 11. We have noticed that this diameter bears a very important relationship to the interspinous diameter situated at a lower level in the pelvic outlet. *These two diameters so closely approach the same transverse vertical plane that for practical purposes one may be considered either perpendicularly below or perpendicularly above the other, as the case may be.* This relationship is noted consistently when the skeletal pelvis is viewed with the plane of the inlet (later to be described) held so that the line of vision is directed at right angles to the point of intersection of the transverse and anteroposterior diameters of the inlet (Fig. 12, note perpendicular relationship between *C, D*, and *C' D'*).

Thus a transverse section of the pelvis through its widest transverse diameter and the ischial spines divides the pelvis into an an-

terior and a posterior segment. The anteroposterior diameters of each segment are termed the "anterior" and "posterior" sagittal diameters for all levels, Figs. 12 and 13,  $A^1$  and  $B^1$ . In practice, however, the inlet or the outlet represents the common level at which a knowledge of these diameters is most significant. The anterior sagittal is almost invariably longer than the posterior sagittal diameter for both the inlet and the outlet. In fact, in certain forms of android types

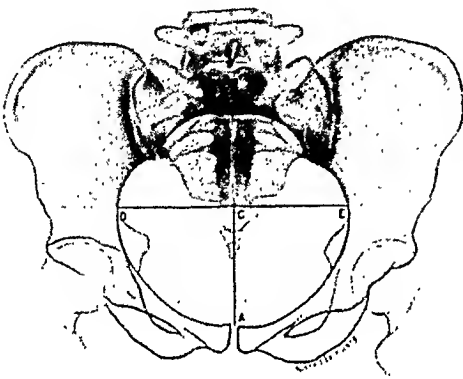


Fig. 8.

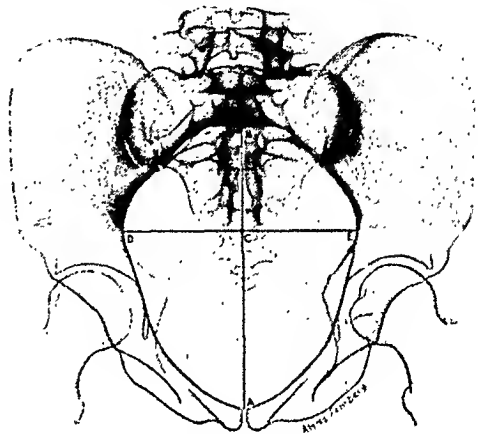


Fig. 9.

Fig. 8.—Gynecoid type. For each pelvic type, Figs. 8 to 11, note that the widest transverse diameter  $D. E.$  intersects the anteroposterior diameter  $A. B.$  at  $C.$ , dividing the latter into two parts: the anterior sagittal diameter  $A. C.$  and the posterior sagittal  $C. B.$  Note the variation in length of each in the four parent types. The perpendicular relation of the widest transverse of the inlet and the interspinous diameter cannot be illustrated due to the slight tilt of the inlet.

Fig. 9.—Anthropoid type. (See legend under Fig. 8.)

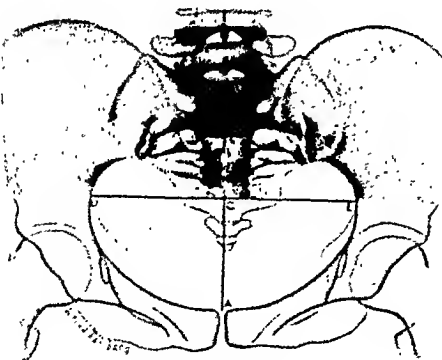


Fig. 10.



Fig. 11.

Fig. 10.—Platypelloid (flat) type. (See legend under Fig. 8.)

Fig. 11.—Android type. (See legend under Fig. 8.)

with anthropoid tendencies, the true conjugate diameter consists chiefly of the anterior sagittal diameter. The characteristic variations in the length of both sagittal diameters at the inlet for each of the four parent pelvic types are illustrated to advantage in Figs. 8 to 11. *In any individual pelvis the length of each is maintained from inlet to outlet, Fig. 13,  $A^1 B^1$*  This point is particularly important

in regard to a clear understanding of the capacity of the anterior and posterior pelvis at the outlet.

Having established this principle and observed that it holds for all types of pelvis, it remains to inquire into the manner in which such established obstetric measurements as the anterior and posterior sagittal diameters of the outlet (Klien) are affected. Note that the anterior sagittal diameter (Klien), Fig. 13, *E. F.*, is really an index

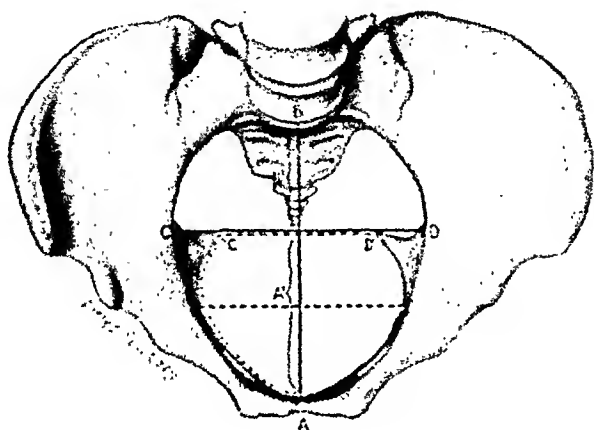


FIG. 12.—Inlet view: Relation between inlet and lower pelvis. Principles apply to all types (anthropoid type illustrated). The widest transverse diameter of inlet *C, D.* is directly above the interspinous diameter *C¹ D¹*. The intertuberos diameter is in front of and considerably below the interspinous diameter and almost invariably longer. The anterior sagittal diameter *A¹* is longer than the posterior sagittal *B¹*.

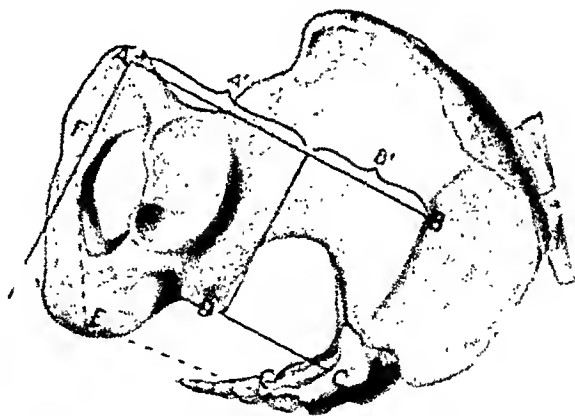


FIG. 13.—Lateral view of Fig. 12. The anterior sagittal *A¹* and the posterior sagittal *B¹* are preserved from inlet to outlet and represent the true index to pelvic capacity for anteroposterior diameters throughout the pelvis. Modified only by variations in the subpubic arch and lower sacral region. Note that the anterior sagittal of Klein *E, F.* represents an index to the perpendicular length of the ischio-pubic ramus, while the posterior sagittal of Klein *F, C* is not as reliable an index to posterior pelvic capacity as the length of *B¹* at higher levels.

to the perpendicular length of the pubic and ischial rami and, therefore, of little obstetrical significance. The capacity of the lower fore pelvis is primarily dependent on the transverse diameters in this region (Figs. 16 to 19). Any measurement of the posterior sagittal diameter of Klein at the outlet cannot be accepted as a reliable index to posterior pelvic capacity at higher levels (Fig. 13, *E. C*). This diameter may be decreased by a forward curvature of the sacral tip

in a normal pelvis to the same degree as it is shortened in an extreme android type, in which the head would be arrested at the inlet. Or again, an increase in the length of the posterior sagittal diameter of Klien may infer either a long anthropoid type of posterior segment in the posterior pelvis or a straight sacrum which is inclined backward. In this latter case, the posterior segment at the inlet may conform to any type. In other words, we are stressing the importance of associating the outlet diameters with the pelvis as a whole in establishing a working prognosis in regard to the mechanism of labor.

In order that the length of the anterior and posterior sagittal diameters of the inlet, as described, may be maintained throughout the pelvis, the sacrum must possess a normal curvature and inclination posteriorly, while the symphysis and pubic rami anteriorly must approach closely the same parallel plane and become straight. Fortunately, this desirable anatomic relationship usually obtains, but this

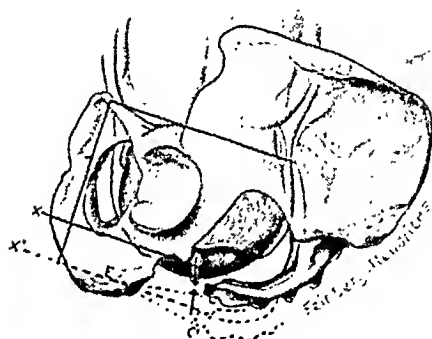


Fig. 14.



Fig. 15.

Fig. 14.—Lateral view. Posterior pelvic capacity at the outlet as modified by lower sacral variations.  $C^1$  forward curvature of sacrum at low level. Compensatory space directly forward at  $X^1$  in lower aspects of subpubic arch.  $C$  represents elevation of forward sacral tip toward region of ischial spine. Loss of compensatory space directly forward at  $X$ , since subpubic arch narrows rapidly toward symphysis in this region. Note that differences in posterior sagittal of Klien,  $E$ ,  $O$ , and  $E$ ,  $C^1$ , give no reliable index to the change in level of sacral tip. Resistance offered head by sacral tip hinders the normal dilatation of cervix (see arrows).

Fig. 15.—Lateral view of fore pelvis. In addition to a decrease in transverse diameters in lower fore pelvis (see Figs. 16 to 19), the deviation of plane of the pubic rami behind the plane of the symphysis may modify lower pelvic capacity in the fore pelvis.

rule is not invariable. It is the departures from the normal which can be expected to modify the mechanism of labor. In the posterior pelvis, lower sacral variations, such as an acute forward inclination or curvature, will decrease the outlet capacity. When this occurs, it is not so much the extent of the forward swing of the sacral tip as it is the amount of elevation of the lower sacral region in relation to the ischial spines, Fig. 14. If the sacrum curves forward at a low level, the mechanism of labor need not be affected materially unless the general pelvic type is distinctly abnormal. The head can descend to this low level where it may utilize, when it moves into the fore pelvis, the space afforded by the widest part of the subpubic

arch at a point directly in front of the lower sacral region. If, however, considerable elevation of the lower sacral area in relation to the ischial spines is present, a bony platform is created in the posterior pelvis which may cause arrest of the head at a higher level. In this case the head cannot move forward because no compensatory space exists directly in front in the narrower upper portion of the subpubic angle. At this higher level, the pubic rami converge toward the under surface of the symphysis and offer a more solid bony resistance to the lateral aspect of the fetal head when any attempt is made to direct

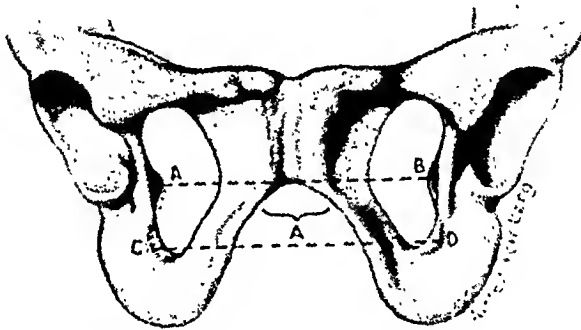


Fig. 16.—A narrow subpubic arch similar in size to Fig. 18. Note wide interspinous (A, B.) and intertuberosity diameters (C, D.).

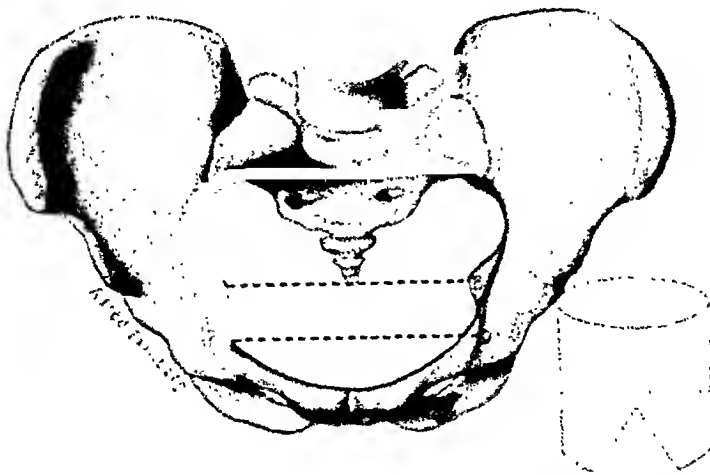


Fig. 17.—Inlet view of pelvis in Fig. 16. Typical android type. Observe that the interspinous (A, B.) and intertuberosity diameters (C, D.) are long and the side walls converge in front of the latter to form a narrow subpubic arch. As a result, the entire fore pelvis is well formed in spite of the narrow subpubic arch (Fig. 16).

the head into the fore pelvis. For each of the two levels of the sacrum illustrated in Fig. 14, the length of the posterior sagittal diameter of Klien ( $E, C$ , and  $E, C'$ ) would give no reliable index to the degree of sacral elevation or the type of obstetrical difficulty encountered.

Labor in pelvis with a forward curvature of the lower sacral region is complicated frequently by failure of the cervix to dilate and retract normally. The cause for this cervical difficulty is explained in Fig. 14. The head, meeting the resistance of the lower sacrum and *coenx* (ar-



rows), is unable to descend far enough at the height of each contraction to bring pressure to bear against the dilatable cervix. As a result, dilatation ceases usually with an appreciable rim of cervix around the head. This abnormality illustrates a principle in the normal dilatation and retraction of the cervix. For this to occur, the head must be permitted to descend with each contraction unobstructed by the bony pelvis at any point, in order to make proper pressure against the cervix and then to recede to a higher level through the elastic recoil of the soft parts as the contraction subsides.

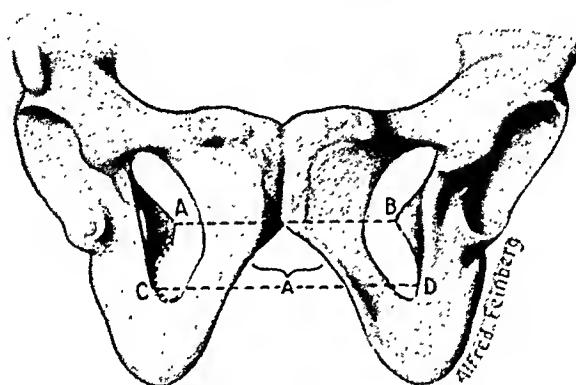


Fig. 18.—Front view of narrow subpubic arch comparable in size to Fig. 16. Note narrow interspinous (A. B.) and intertuberosity diameters (C. D.).

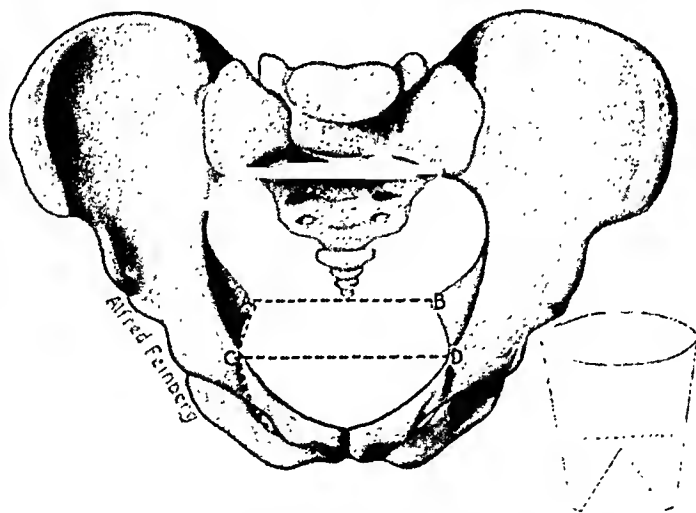


Fig. 19.—Inlet view of pelvis in Fig. 18. Typical anthropoid type. The lateral pelvic walls converge to the narrow arch, causing a decrease in both the interspinous (A. B.) and intertuberosity diameters (C. D.). Thus, Figs. 16 to 19 show that the size of the subpubic arch gives no indication of the type of pelvis which may be associated with it.

Invariably, the anterior sagittal diameter in the midline is maintained from inlet to outlet. Pelvic capacity in the fore pelvis is affected chiefly by a decrease in the transverse diameters in front of the ischial spines, Figs. 16 to 19. Marked deviation of the plane of the pubic rami behind the plane of the symphysis, however, represents a condition which occurs frequently in narrow fore pelvises, Fig. 15. Under such circumstances, the pubic and ischial rami not only

hinder rotation but prevent the occiput from attaining the position close to the posterior plane of the symphysis, so essential for descent in the axis of the fore pelvis. Accordingly, the head must descend through the narrow fore pelvis in an axis more posterior to the usual axis, thus forcing it against the coccyx and resistant sacrospinous ligaments of the lower posterior pelvis.

At the inlet, when the widest transverse diameter is narrow, the pelvis, as a rule, is anthropoid in type with characteristic effects on the mechanism of labor. Likewise, narrowing of the interspinous diameter at the outlet will exert a characteristic influence in hindering the normal rotation of the fetal head, since this diameter has the same relation to the outlet as the widest transverse diameter bears to the inlet. But narrowing of this diameter does not imply that the pelvis conforms to any special type, because definite narrowing may occur at the interspinous diameter in any type of pelvis, and it is the presence or absence of convergence of the side walls from the inlet which is especially important, i. e., whether the convergence is present in the region of the ischial spines or more anterior in the fore pelvis (see Figs. 16 to 19).

The relationship of the interspinous to the intertuberous diameter must also be considered. *The intertuberous diameter is always in front of the interspinous and at a considerably lower level, Fig. 12. Also, almost invariably the intertuberous is wider than the interspinous.* This fact makes the interspinous diameter, rather than the intertuberous, the index to transverse capacity in the lower pelvis. It must be realized, of course, that the intertuberous and interspinous diameters may be normal in size and yet an abnormality may exist at the inlet on which the prognosis depends.

No description of the abnormal pelvis is complete without reference to the narrow subpubic angle. As we had occasion to study more cases with a complete roentgenologic and obstetric work-up, we began to observe that patients with a narrow subpubic angle would frequently deliver normally without extensive laceration, while others encountered more serious difficulty. It became obvious that the size of the subpubic angle in itself represented no reliable index to the ease or difficulty encountered, even when narrowing existed. The first important factor has already been referred to in that the basic pelvic type is important. If the posterior sagittal diameter at the inlet (as in android types), is short, this shortening is carried down through the pelvis, so that the index to the capacity of the posterior pelvis is the measurement at the inlet rather than the length of the posterior sagittal diameter of Klien at the outlet. The other factors are the length of the intertuberous and interspinous diameters

and the point of maximum convergence of the side walls. These features are illustrated in Figs. 16 to 19. Both pelves illustrated possess equally narrow subpubic angles. The type of pelvis, however, behind the subpubic angle is radically different in the examples illustrated, and each pelvis predisposes to a radically different mechanism of labor. Note that the pelvis in Figs. 16 and 17 (front and inlet views) represents a typical android with a wide interspinous and intertuberous diameter, but the fore pelvis converges rapidly in front of the latter diameter to form the narrow subpubic arch. Thus, the fore pelvis of this example is well formed and ample, in spite of the narrow pubic arch. In this case, an average-sized child was delivered spontaneously after a shallow episiotomy. The pelvis in Figs. 18 and 19, however, conforms to the anthropoid type, in which the interspinous and intertuberous diameters are both narrowed. The lateral walls of the pelvis in this case converge rapidly from the inlet to the outlet, decreasing both the intertuberous and interspinous diameters. In this case, the persistence of a posterior position necessitated medium forceps delivery, in spite of the fact that the child was under average in size and the posterior sagittal diameter of Klien was long.

It is thus evident that no prognosis of the difficulty likely to be encountered at the outlet can be made without precise knowledge of the character of the pelvis as a whole, for on this depends the way in which the head is going to reach the outlet.

## 2. THE TRUE CONJUGATE DIAMETER; ITS PERPENDICULAR LINE AND RELATION TO PELVIC PLANES

Obstetric pelvimetry makes use of the sacral promontory as the posterior origin of the obstetric conjugate diameter of the inlet, while its anterior origin is defined as a point in the upper posterior curved edge of the symphysis. From the experience gained by a careful study of large numbers of skeletal pelves in museums, and from this large series of complete roentgenologic examinations on living women, we believe that the promontory is too unstable in position in relation to the plane of the inlet to be used as a point of origin of such an important obstetric diameter. This posterior point should be in the midline of the lower anterior surface of the first sacral vertebra where the continuation of the iliopectineal lines on either side meet each other, Fig. 20. When a line is drawn from this intersection to the point at the symphysis described above, the "available obstetric or true conjugate diameter" is not only defined in a manner standard for all pelves, but it also denotes the level of the first obstetric plane of the pelvis.

A perpendicular through the midpoint of this true conjugate diameter and first plane of the pelvis invariably points downward

through the center of the pelvis. In a few pelvises, this perpendicular line may coincide with the central pelvic axis, but only when the plane of the symphysis and plane of the anterior upper sacral surface display a right-angled relationship to the true conjugate diameter. As a rule, the planes of the symphysis and sacrum slope posteriorly, and under these circumstances the perpendicular line by no means indicates the static axis of the pelvis. Its main purpose is merely to indicate the mean direction of descent through the true pelvis and to afford a means of determining the angular relationship of the head to the pelvic cavity, by defining clearly the direction in which it points for any level in the pelvis (Fig. 20, small arrows). It is the relationship of this line to the long axis of the head which indicates

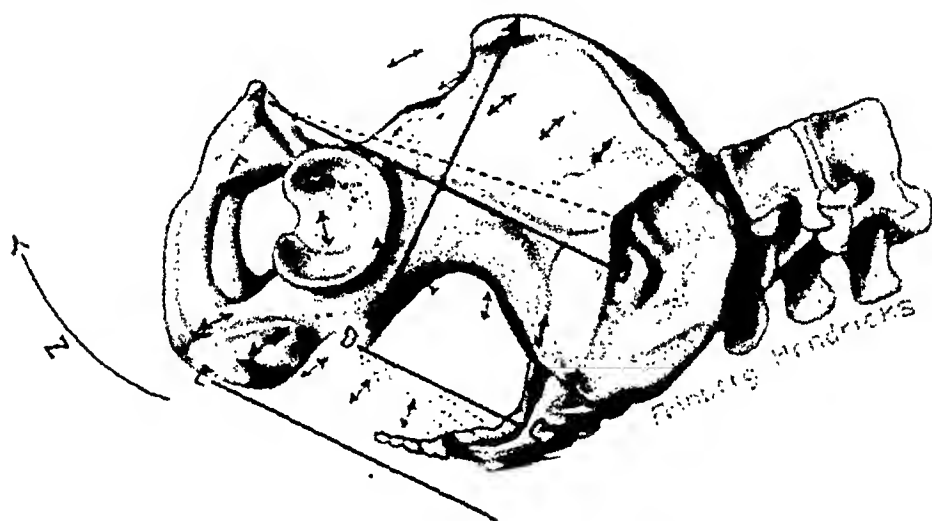


Fig. 20.—Parallel planes (after Dodge<sup>4</sup>) and perpendicular line at inlet. A. B., Available obstetrical or true conjugate diameter and first parallel plane. A. B., Anatomical conjugate diameter from sacral promontory. D. C., Second parallel plane. E., Third parallel plane. Z., Axis of extension. Note varying angular relation of fetal axis (small arrows) for three important levels of the pelvis in relation to the perpendicular through midpoint of A. B. (The perpendicular indicates the mean axis of descent.)

the presence or absence of synclitism (review Figs. 1 to 7). Any perpendicular line to the true conjugate would serve the same purpose, but the midpoint is most easily located.

From a practical standpoint, it is important to be able to follow and demonstrate the curve of descent of the head through the upper pelvis to the bottom of the posterior pelvis. The spines and interspinous diameter become reliable landmarks from which the spacial relationship of the head can be determined at all levels. The median sagittal suture of the fetal head for O T positions, or a point on it near the posterior fontanel, may be chosen as fixed regions of the head to compare with the static pelvis. It is realized, of course, that during vaginal examination in the individual case these points may

be obscured from molding, in which event other points on the head may be recognized and used for the same purpose. If the head has descended to the level of the spines and the median longitudinal suture is situated slightly in front of the interspinous diameter, it can be assumed that at that particular level the head is fitting squarely in the pelvic cavity. This assumption follows because the ischial spines are usually situated behind the center of the inlet. As described above, the anterior sagittal diameter, at this or any level, is always longer than the same posterior diameter. It extends to a point perpendicularly below the point of intersection of the transverse and anteroposterior diameter at the inlet. Whereas, if the sagittal suture points into the center of the fore pelvis considerably in front of the spines, Fig. 35, or backward at or slightly behind the ischial spines, Fig. 6, a lateral roentgenogram will reveal a head asynclitic to the perpendicular to the inlet.

The second plane of importance extends parallel with the first, from the level of the ischial spines to cut the lower segments of the sacrum at the point where the fourth and fifth segments normally slope forward to form the forward curvature of the lower birth canal *C. D.*, Fig. 20. This lower gutter is created by the fanlike sacrospinous ligaments on either side, spreading from the ischial spines to their insertion along the lower lateral border of the sacrum and the lateral aspects of the coccygeal vertebra, Fig. 20. This second plane is similar to the third parallel plane of Hodge<sup>4</sup> and has been chosen because arrest commonly occurs at this level.

The sacral tip and coccyx form the bottom of this trough which, in the main, may be considered a platform within the posterior pelvis, which is anatomically at a slightly higher level than the third or last parallel plane through the lowest extremity of the ischial tuberosities, Fig. 20, *E*. Normally, the pelvic surface of the coccyx and sacral tip is placed midway between the second and third parallel plane, and extends forward almost to the midpoint of the interspinous diameter. The point of origin of these pelvic planes is constant for all pelves, but the distance in levels with respect to each other, as well as the anteroposterior or transverse diameters of each plane, changes in accordance with depth and shape of the individual pelvis.

### 3. THE PELVIC SOFT PARTS

Having observed that the fetal head descends in a curved direction from the region of the symphysis toward the bottom of the true pelvis, we became interested in the possibility of an explanation in the pelvic soft parts rather than in the bony pelvis. This curve of descent is especially noticeable in normal efficient labor. Unquestionably, the forward excursion of the uterus with a contraction carrying with it the entire fetal axis is very important in directing the head

backward, since, during a contraction, the fetal head and body become a straight line, and the axis of drive downward is in the general axis of the fetal piston. Between contractions the long axis of the fetal head, and its changing asynclitic or angular relationship to the pelvis during this downward and backward curve of descent, can be assumed also to represent the relative direction of the forward excursion of the fetal axis when a contraction occurs. It is easy to demonstrate "posterior lateral flexion" by roentgenologic methods because, as the uterus relaxes, the fetal body sags against the mother's vertebral column, while the head is relatively fixed by the soft parts of the lower pole of the uterus. However, the lower pole of the uterus and adjacent soft parts likewise must exert an important influence in directing and maintaining the descent of the head downward and backward into the more ample posterior pelvis, at the same time promoting flexion of the head. Flexion, of course, is chiefly caused by the uniform resistance offered to the head by the normal tonicity of the lower uterine segment and cervix, as these structures dilate and retract. It must be realized that the anterior lower pole of the uterus is reinforced by strong fascial support anteriorly, the urinary bladder, and finally the unyielding bony symphysis and upper portions of the pubic rami. While we may suggest that the lower pole of the uterus assists in directing the fetal head downward and backward, we infer, of course, that it is augmented by the bony and fascial structures surrounding it, but especially those in front. Collectively, these factors afford sufficient resistance to the head, as it descends by the force of the straight uterine drive along the fetal piston, to deviate it slowly backward with contractions. The lower pole of the uterus, even alone, plays no small rôle in this directing mechanism. So far as we have been able to determine, the axis of the lower pole of the uterus is directed more in the axis of the posterior pelvis than in the fore pelvis, indicating the remarkable precision of anatomic structure, in that soft parts and hard parts appear to be so arranged as to gain the maximum in physiological effort. In the accompanying diagram, Fig. 21, the direction of the axis of the lower uterine segment and cervix will be found to point toward the lower posterior pelvis, avoiding the lower fore pelvis. It will also be observed that the fetal head, descending in line with the axis of the uterus, will be deviated backward by the resistance afforded by the structures anteriorly at A, Fig. 21.

If the soft parts in the upper pelvis represent at least one of the factors which allow the head to descend to the bottom of the posterior pelvis to a region confined by the two ischial spines and the lower sacral region and coccyx in the midline, the muscular struc-

tures of the perineum and pelvic diaphragm under the subpubic arch can be expected to influence the descent of the head through the lower fore pelvis and vulva. In Fig. 22 an attempt has been made to illustrate several important points regarding the relationship of the muscular attachments at the outlet. The pelvis has been sectioned laterally, just medial to the ischial tuberosities. Note first that the true pelvis approaches the form of a parallelogram, and that the bony depth anteriorly and posteriorly is almost equal. The levator diaphragm is practically parallel with the inlet, while the muscles supporting the vulva within the confines of the subpubic arch are, for practical purposes, at right angles to the levator sling (compare *A* with *B* and *C*, Fig. 22).

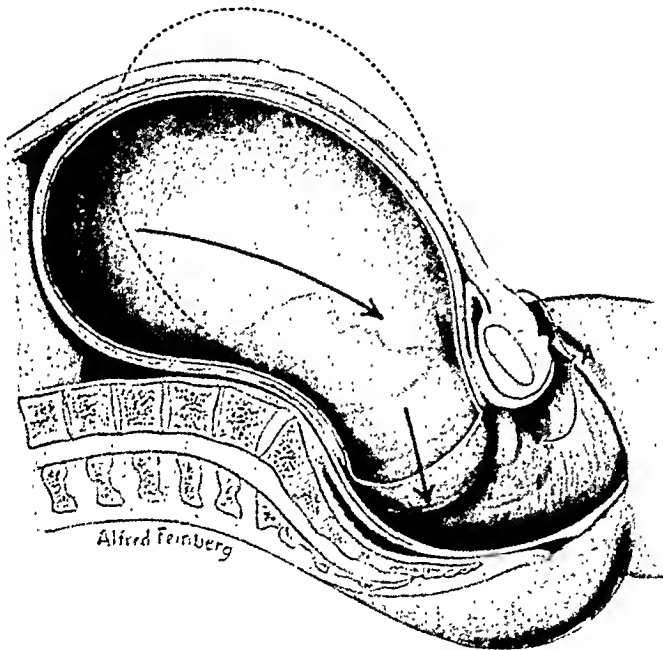


Fig. 21.—Relation of axes of soft parts of uterus and its lower pole to the static pelvis at the inlet. The axis of the uterus proper is downward and forward against the fascial and bony structures in front of the lower pole at "A." The axis of the lower pole (lower uterine segment and cervix) agrees with the axis of the posterior pelvis. We believe this soft part axis aids in permitting the head to descend and utilize the more available posterior pelvis.

An explanation of the significance of this anatomical arrangement in labor is assisted by reference to Hart's pubic and sacral segments of the pelvic outlet. During labor, as the head descends into the posterior pelvis, retraction and dilatation of the cervix occur, elevating the anterior vaginal wall, bladder, and other soft structures in the fore pelvis. At the same time, the soft structures of the pelvic outlet behind and below the posterior vaginal walls are dilated slowly, first in the posterior aspects of the pelvis adjacent to the lower part of the sacrum and coccyx, and the sacrospinous ligaments laterally. The head soon meets the resistance of this bony-ligamentous barrier (Fig. 22, *C*), cannot descend lower, and so moves forward and down-

ward by a series of up-and-down movements during contractions. As soon as the head passes in front of the coccygeal tip, only the soft parts of the levator sling and perineum are encountered (*B*, Fig. 22), and with each contraction the fetal head descends to bulge this region in the lower fore pelvis. When the perineum is distended to the maximum, the muscles of the subpubic arch and vulva, placed at a slightly higher level and at right angles, make it necessary that the head extend upward to pass under the arch in the terminal aspect of the delivery. In Fig. 22, note that the transverse muscles of the pelvic diaphragm, originating near the ischial tuberosity (junction of *A* and *B*), would normally be dilated and stretched by the head descending through the intertuberous diameter. If, however, the head were not directed at the proper angle against these strong mus-

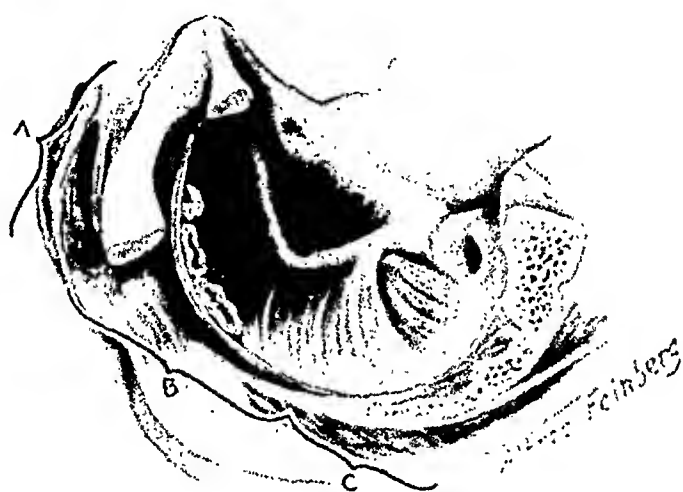


Fig. 22.—Soft parts of pelvic outlet. Note that the true pelvic cavity approaches the form of a parallelogram. The levator sling is almost parallel with the inlet. *A*, represents the vulva and pelvic diaphragm and other structures in the subpubic arch. *B*, represents the dilatable obstetric perineum. *C*, represents the lower curved sacral region which is resistant to descent below this level. Note the right-angled relationship of "*A*," to "*B*," and "*C*," with the strong transverse muscles of the pelvic diaphragm at junction of "*A*," and "*B*," and at a slightly higher level than "*B*."

cles, extension might occur too soon. The common occurrence of this feature explains why episiotomy is done frequently at the outlet.

The conception of a soft part axis, as distinct from the static axis of the bony pelvis, is not new. Fabbrì, Sabatier, Pinard,<sup>5</sup> Parvin<sup>6</sup> and others called it the "dynamic axis" of the pelvis, but did not stress the importance of the lower pole of the uterus.

#### 4. PELVIC AXES

The pelvic axis, for the most part, has been determined on the assumption that the depth of the fore pelvis is represented by the width of the symphysis, and that of the posterior pelvis by the long anterior surface of the sacrum. When it is realized that the true pelvis approaches the form of a parallelogram, as we have already



described, the "curve of Carus" can by no means represent the axis of the static pelvis. Hodge<sup>4</sup> and others realized that the upper portion of the axis at least was represented by a straight line to the region of the ischial spines, and concluded that the perpendicular axis of the inlet represents this straight axis of descent followed by the fetal head.

On the basis of this investigation, a diagram to illustrate the axis of descent of the fetal head would be arranged as in Fig. 23. The axis of the line of descent, illustrated diagrammatically in Fig. 23, is formed by joining similar points on the series of fetal heads. The shape of this curve varies in relation to the pelvis in each individual case, but the average curve simulates the axis illustrated. This dia-

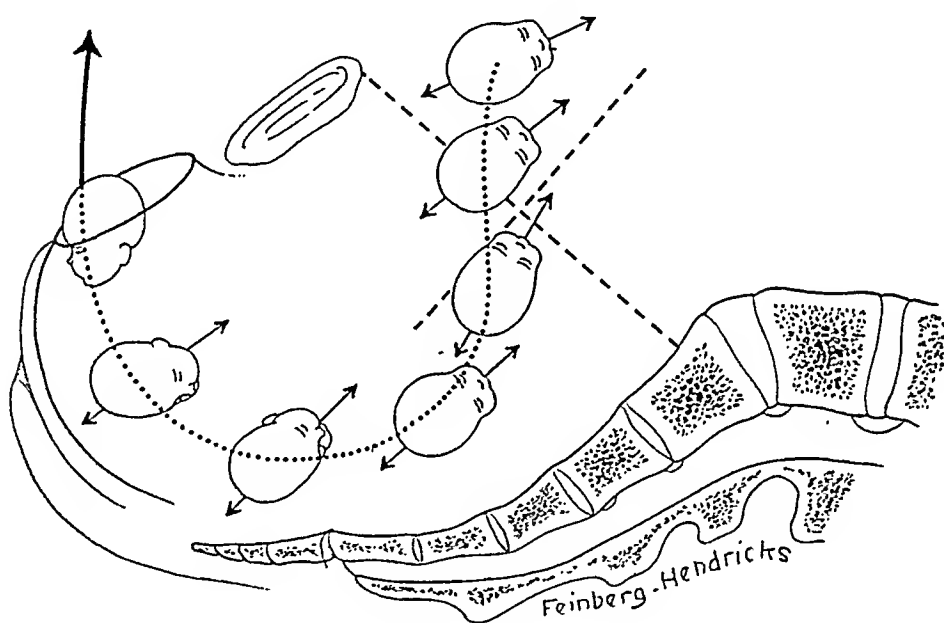


Fig. 23.—Diagram illustrating the axis of descent as revealed by this investigation. The dotted line joining similar points on the series of fetal heads reveals the general character of the axis. Note the angular relationship between the fetal axis and the perpendicular axis of the pelvis, and the difficulty of anatomically associating the relation of head to pelvis at any given level. The fetal piston moves upward and downward in a straight line with each contraction. Note relationship of its position to the static pelvis at the following levels: (1) During engagement from a posterior parietal position at the inlet. (2) At low level in posterior pelvis (see Fig. 24, C. D.). (3) Shift forward with descent along inclined plane of outlet. (4) On perineum to distend it by straight drives downward in axis of fore pelvis (see Fig. 24, G. F.).

gram will show the great difficulty of associating varying angular relationship of the long axis of the head to any axis of the static pelvis, from the fact that the head follows an axis which, for any given position, bears no constant anatomic relationship to the pelvis until the head is fixed under the pubic arch in the axis of the soft parts of the pelvic outlet.

There are, however, two levels in the pelvis for which a static axis may be described and through which the head passes in normal labor or must be made to pass if, in ease of arrest, forceps delivery becomes

necessary. These two axes are illustrated in Fig. 24. The first of these is the axis of the posterior pelvis which originates at *C*, the point of intersection of the widest transverse diameter with the true conjugate diameter at the inlet, and descends parallel to the sacrum. The head may utilize this axis from the beginning of labor in some cases, but, as a rule, when there is a posterior parietal position at the inlet, with the long axis of the head and fetus directed downward and forward in the fore pelvis, it must first swing downward and backward. Under these circumstances, the axis of the posterior pelvis, as described, is not used by the head in the upper pelvis, but only for a short and variable distance in the posterior lower pelvis near the sacrum. From a practical standpoint, it is at this level that arrest of the head is prone to occur, and hence the axis of the posterior pelvis, as described (*C. D.*, Fig. 24), must be appreciated when traction by forceps is used.

After rotation has occurred in the inclined plane of the outlet, a common position for arrest to occur is between the second (ischial spines) and third parallel planes (ischial tuberosities) in the fore pelvis, with the head close to or on the pelvic floor. In normal labor, the head also descends through this axis. The axis of the fore pelvis may be defined as a line originating at the center of the anterior sagittal diameter of the inlet at *E*, Fig. 24, and descending parallel to the posterior surface of the symphysis, *E. P.* Here again, only the lower part of the axis is normally used by the head, usually the short distance between *G. F.*, Fig. 24.

When a head is arrested in the upper midpelvis and forceps are indicated, the line of traction should avoid the axis of the fore pelvis, just described, and follow the physiologic curve of descent (the upper curved axis of descent as in Fig. 23) downward and backward toward the sacrum, ultimately using the axis of the posterior pelvis (*C. D.*, Fig. 24).

Two conceptions of the axis of the pelvis, as described by other workers, are illustrated in Fig. 25 *A* and *B*. The first obvious difference between these conceptions and those revealed by this investigation refers to the point of origin of the axis at the inlet; whether it should originate at the center of the superior strait, or at a more posterior point representing the intersection of the widest transverse and anteroposterior diameters (*C*, Fig. 24). In all pelvic types, the posterior segment of the inlet is always wider than the anterior segment, and the head normally makes use of this anatomic fact. Moreover, the lower pole of the uterus and its adjacent structures assist in deviating the head backward in this direction. Hence the pelvic axis should originate at the point we have described. Since the fore pelvis is too far removed at this high level to influence the direction of the axis

from this point, the inclination of the sacrum rather than its curvature must represent the anatomic factor most significant in the determination of this direction. As we have noted, a line parallel to the sacrum can be defined easily anatomically as the axis of the posterior pelvis (*C. D.*, Fig. 24).

Except for its central point of origin at the inlet, the upper part of the "curve of Carus," in direction at least, is comparable to the

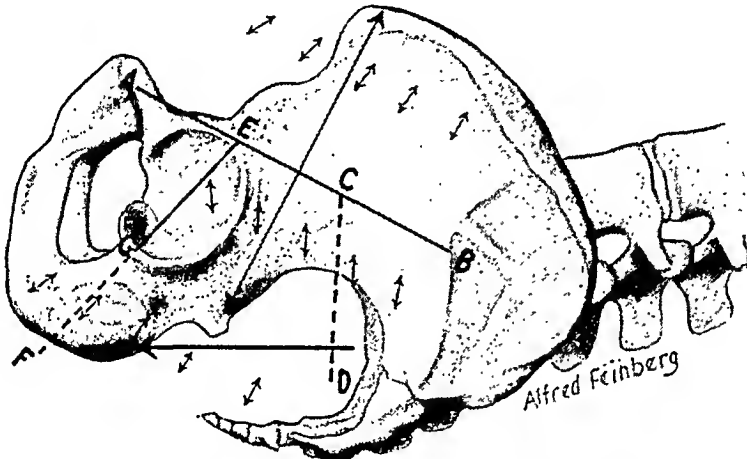


Fig. 24.—Anatomical axes of true pelvis. *C.*, Point of intersection of widest transverse and anteroposterior diameters of inlet. *A. C.*, Anterior sagittal diameter. *C. B.*, Posterior sagittal diameter. *C. D.*, Axis of posterior pelvis originating at "*C*" and descending parallel with upper segments of the sacrum. Head utilizes lower aspects of this axis after engagement from the posterior parietal position. *E. F.*, Axis of fore pelvis originating at "*E*," the midpoint of the anterior sagittal. The head utilizes lower portion of the axis *G. F.* after it has moved forward in direction of heavy arrow. The perpendicular line indicates the "mean" direction of descent, but the head usually bears an angular relation to it for different levels (small arrows).

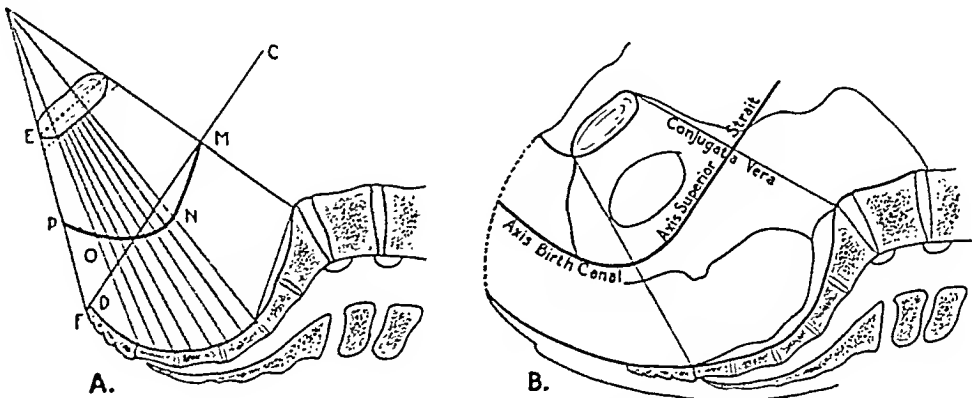


Fig. 25.—Two theories of the static pelvic axis. (A) "Curve of Carus" (redrawn from Bedford<sup>9</sup> 1861) representing the midpoint of planes from symphysis; *C. D.*, Axis of superior strait. *E. F.*, Plane of inferior strait. *M. N. P.*, Central curved line. Earlier obstetricians assumed that the width of the symphysis formed the anterior boundary of the true pelvis rather than the entire depth of the fore pelvis. (B) Straight axis perpendicular to inlet to level of spines. (Redrawn from Williams<sup>10</sup> 1930.) This theory does not regard the relationship to the inclination of the sacrum. Other authorities have pointed out this fact, but failed to define the axis clearly from the anatomical standpoint.

axis of the posterior pelvis as described (compare Fig. 25, *A* with *C. D.* of Fig. 24). A perpendicular from the inlet, however, does not consider the inclination of the sacrum, and therefore cannot repre-

sent the axis of the pelvis, except in certain pelves possessing a sacral inclination parallel to this perpendicular. This parallel relation, for instance, does not obtain in the diagram illustrated in Fig. 25, *B*.

We have already referred to the variable direction this perpendicular will assume, even when the plane of the inlet is made to correspond with a standard "available obstetrical or true conjugate diameter." The variable position of the promontory will further modify the relationship of any perpendicular axis to the true pelvis whenever the promontory is used as a point of origin of a diameter from which the perpendicular is drawn. These significant factors may be seen to advantage in Fig. 25, *A* and *B*.

Traction with forceps may be safely applied in the central axes of normal pelves (as in Fig. 25) and very flat forms, because in certain examples of the latter type the widest transverse diameter may bisect the anteroposterior diameter of the inlet. The importance of utilizing the axis of the posterior pelvis (Fig. 24, *C*, *D*.) becomes apparent if the fore pelvis is narrow, in which event traction along this axis allows the head to descend to a low level in the posterior pelvis by avoiding the abnormality present in the fore pelvis. If, in such a case, traction is made in the central axis of the pelvis, the head is angulated away from its physiologic axis in the posterior pelvis and directed into the narrow fore pelvis at a higher level, thereby greatly increasing the difficulty.

Milne Murray,<sup>7</sup> Hirst<sup>8</sup> and others have agreed that the axis of the pelvis is determined by the inclination and curvature of the sacrum, but this relationship has always been associated with the perpendicular of the superior strait or the center of line radiating from the symphysis, as in Fig. 25, *A*. As we have noted above, no stable relationship can be defined from such a premise, even though the relationship of the pelvic axis to the sacrum is correct.

The lower part of the "curve of Carus," Fig. 25, *A*, or a similar forward curve in the lower part of the axis in Fig. 25, *B*, does not represent the axis followed by the head at this low level, because, as it moves forward from the bottom of the posterior pelvis, the head is still confined by the pelvic parallelogram and must descend straight downward in the axis of the fore pelvis, as designated in Fig. 24, *E*, *F*. The head can make use of such a forward curvature only after descent has occurred to bulge the perineum to the maximum. As the act of extension begins, the head is fixed in the dilated birth canal under the pubic arch. Only under these circumstances does the occiput swing upward in a curved direction, somewhat comparable to the lower curved part of the axis illustrated in Fig. 25, *A* and *B*.

## 5. THE NORMAL MECHANISM OF LABOR

Many factors concerned in the normal mechanism of labor have already been described. It remains to apply the principles outlined above. In a series of semidiagrammatic illustrations we have attempted to reveal the relationship of the head to the pelvis, at the inlet, at the bottom of the posterior pelvis, in the lower fore pelvis, and finally the mechanism at the outlet, so far as we have been able to visualize the process. A gynecoid or normal female pelvis has been used in these illustrations, Figs. 26 to 37.

When the pelvis is normal and the child is average in size, it is doubtful if the bony pelvis plays a very significant rôle in the mechanism of labor. Yet, under these circumstances, as well as with abnormal pelvises, we have consistently observed that the general axis of descent just outlined is followed. With the soft parts of the birth canal directing the fetus at each level along the optimum anatomical axis of the pelvis and through the most ample diameters, the perfection of natural labor is attained.

In Figs. 26, 27, and 28 the axis of the fetus will be recognized as conforming to the posterior parietal tendency at the inlet for the anterior, transverse, and posterior positions. The uterine thrust with each contraction directs the fetal head downward and forward toward the fore pelvis. As labor progresses, the fetal and uterine axes move forward more perpendicular to the inlet. With each contraction, however, the fetus moves forward and downward in a straight line, so that the anterior portion of the lower pole of the uterus, reinforced in front by strong fascial supports, bladder, and more remotely the bony symphysis, receives the impact of the fetal head. Thus, coincident with descent, the median suture (demonstrated to best advantage in the O T position) slowly moves away from the region of the symphysis toward the mid- and posterior pelvis, constituting a movement which may be termed "posterior lateral flexion." Precisely the same movement or rotation around the central point of the fetal head takes place in anterior and posterior positions. By this movement an original posterior parietal position squares itself into the inlet by fixation of the head against the promontory or upper sacral region posteriorly, as the anterior parietal descends behind the symphysis. Thus, at a certain level in the upper midpelvis, as the head is brought more and more under the influence of the normal tenseness of the lower uterine segment and cervix, the long axis of the head is gradually deviated downward and backward toward the bottom of the posterior pelvis, Figs. 29, 30, and 31. As the head descends lower into the true pelvis, the anterior parietal bone in transverse presentations becomes more easily palpable. It would seem that this observation led Nägele and others to stress the frequency

of this position and to assume that at the inlet this position was the rule. It will be noted, however, that, while the position may be primary in the rare type of ease in which the axis of the fetus at the onset of labor is anterior to any perpendicular line from the inlet (as in Figs. 2 and 4), for the most part, this lower anterior parietal position represents a phase in the movement of posterior lateral flexion from an original posterior parietal position at the inlet. Thus, under the guidance of the lower uterine segment and more remotely the shape of the fore pelvis at the inlet, the fetal head, originally pointing

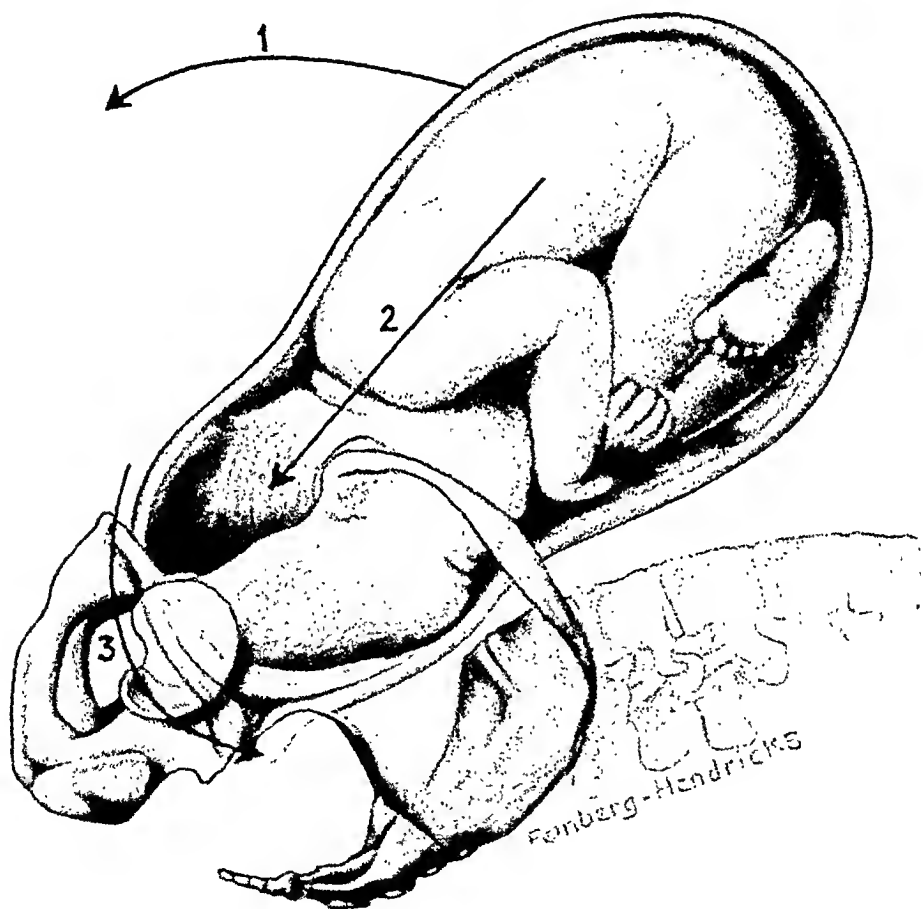


Fig. 26.—Normal mechanism of labor. Engagement from the posterior parietal position (anterior position). (1) Uterus and fetal axis moves forward. (2) Straight drive of uterus along fetus forward and downward. (3) Deviation of head downward and backward from influence of lower pole of uterus, assisted by fascial and bony support anteriorly.

downward into the fore pelvis, by continual straight thrusts of the uterine contraction, is slowly carried backward toward the posterior lower pelvis and close to the sacrum (Figs. 29, 30, and 31) in the axis of the posterior pelvis, Fig. 24.

It will be noticed in these illustrations that at this stage the head avoids the fore pelvis and continues to do so until it meets the resistance offered by the platform of the ischial spines and the lower sacrum and coccyx. This obtains even in cases in which the fore

pelvis is narrowed. It will also be observed in Figs. 29, 30, and 31 that the long axis of the head at this low level tends to be posterior to the perpendicular axis of the inlet. Usually at this level the cervix has attained almost complete dilatation, and since the head cannot descend farther in this downward and backward direction, owing to the resistance of the posterior bony pelvis, it begins rotation from the transverse or posterior positions into the muscular gutter of the pelvic floor.

The head is forced against this inclined pelvic floor by a series of straight thrusts which carries it downward and forward into the fore

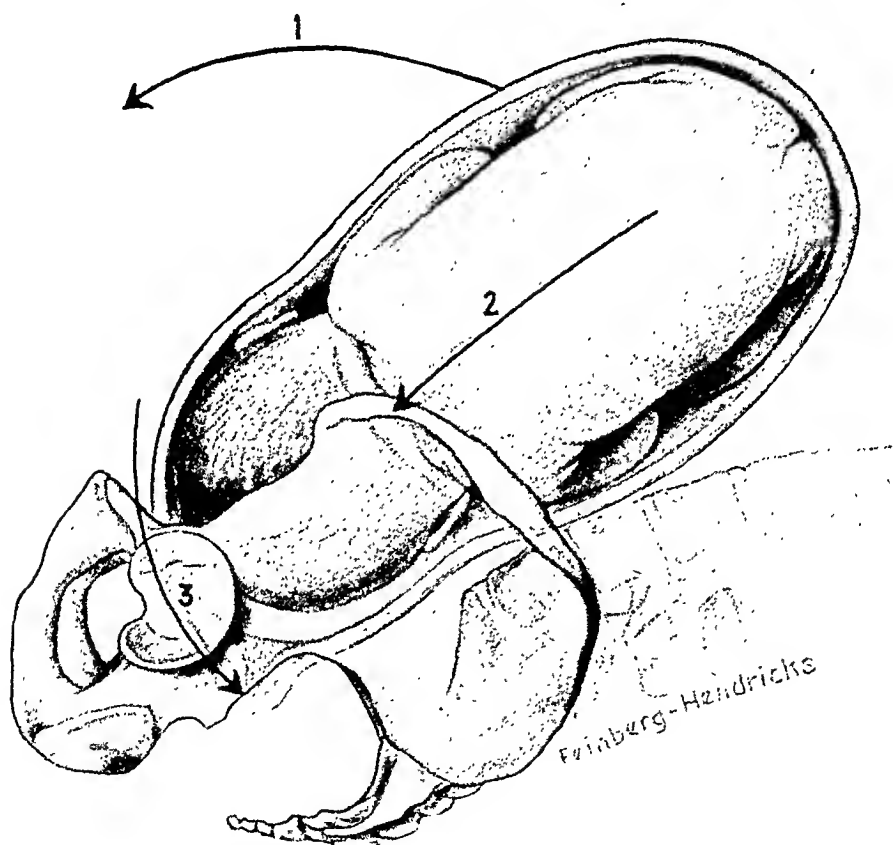


Fig. 27.—Normal mechanism of labor. Engagement from the posterior parietal position (transverse position). (1) Uterus and fetal axis moves forward. (2) Straight drive of uterus along fetus forward and downward. (3) Deviation of head downward and backward from influence of lower pole of uterus, assisted by fascial and bony support anteriorly.

pelvis. From this point it descends more directly against the dilatable perineum in the axis of the fore pelvis. *F. G.*, Fig. 24. Normally, so far as we have been able to observe, extension does not begin at this level, Figs. 32 and 33. In fact, quite the contrary occurs, namely, flexion, as the anterior fontanel and region of the forehead comes in contact with the lower sacral tip and coccyx and the sacrospinous ligaments posteriorly. The pelvic floor acts as an inclined plane, bringing the head close to and parallel with the plane of the posterior surface of the symphysis so that the finger cannot be passed upward

between the head and the bone in this region, while formerly, when the head was in the lower posterior pelvis, considerable space existed in this region. Even when the caput is bulging the perineum at the height of a contraction, the head may recede upward to the low mid-pelvis between contractions, but the entire fetal axis has changed from its former position (compare Figs. 29, 30, and 31 with Fig. 32).

Occasionally, as the head descends in the fore pelvis, the lower portion of the uterus, adapted to maintain the head close to the sacrum, as in Figs. 29, 30, and 31, will cause extension of the head between

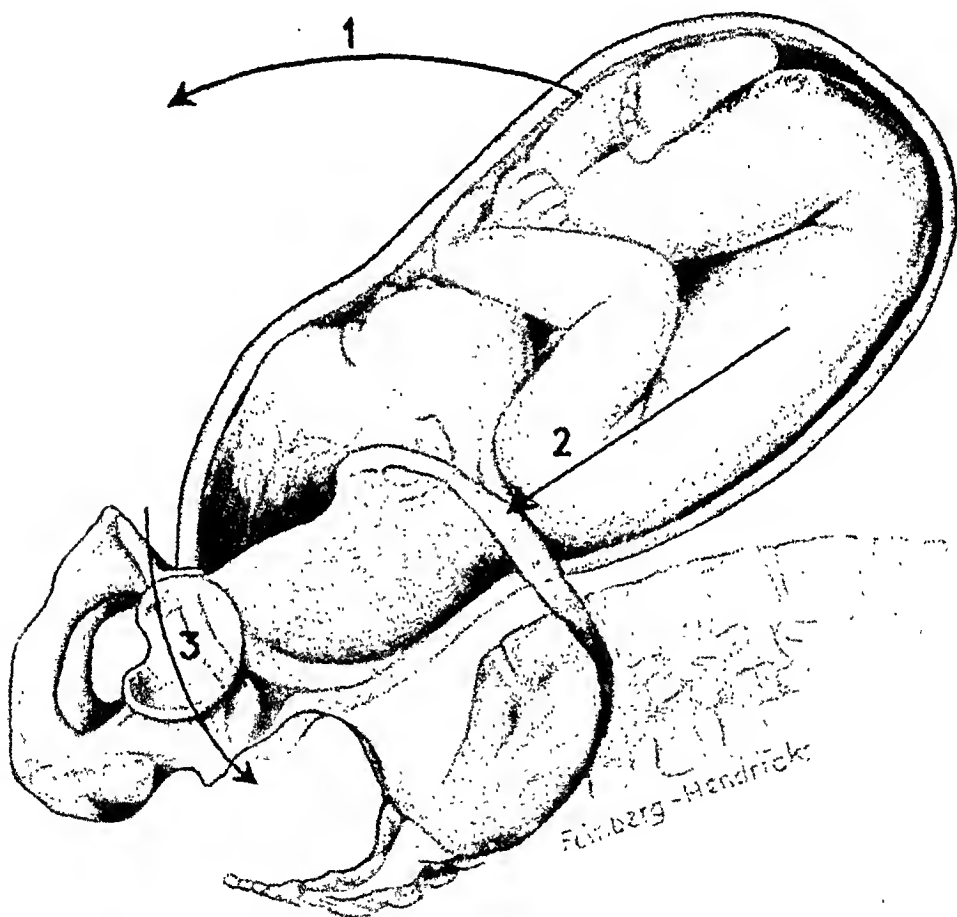


Fig. 28.—Normal mechanism of labor. Engagement from the posterior parietal position (cephaloposterior position). (1) Uterus and fetal axis moves forward. (2) Straight drive of uterus along fetus forward and downward. (3) Deviation of head downward and backward from influence of lower pole of uterus, assisted by fascial and bony support anteriorly.

contractions, as illustrated in Fig. 34. But, with the onset of a contraction, this restraint on the part of the dilated cervix is not sufficient to prevent the back from becoming straight, as in Figs. 32 and 33.

If a transverse position has been maintained to the bottom of the posterior pelvis, on account of the presence of an android posterior pelvis at the inlet, it will be found that the sagittal suture slowly moves forward with descent to correspond eventually with the center



of the fore pelvis. This movement, in which the axis of the fetal head assumes the axis of the lower fore pelvis (*G. E.*, Fig. 24), may be termed "anterior lateral flexion," Fig. 35. This is the movement imparted to the head by the cephalic application of forceps, even before any traction is attempted, as the posterior blade of the forceps cannot avoid angulating the long axis of the head away from the low posterior pelvis into the fore pelvis.

Posterior positions, which have descended to the level shown in Fig. 31, rotate spontaneously, passing through a phase of lateral flexion, descent, and spiral rotation to the anterior position.

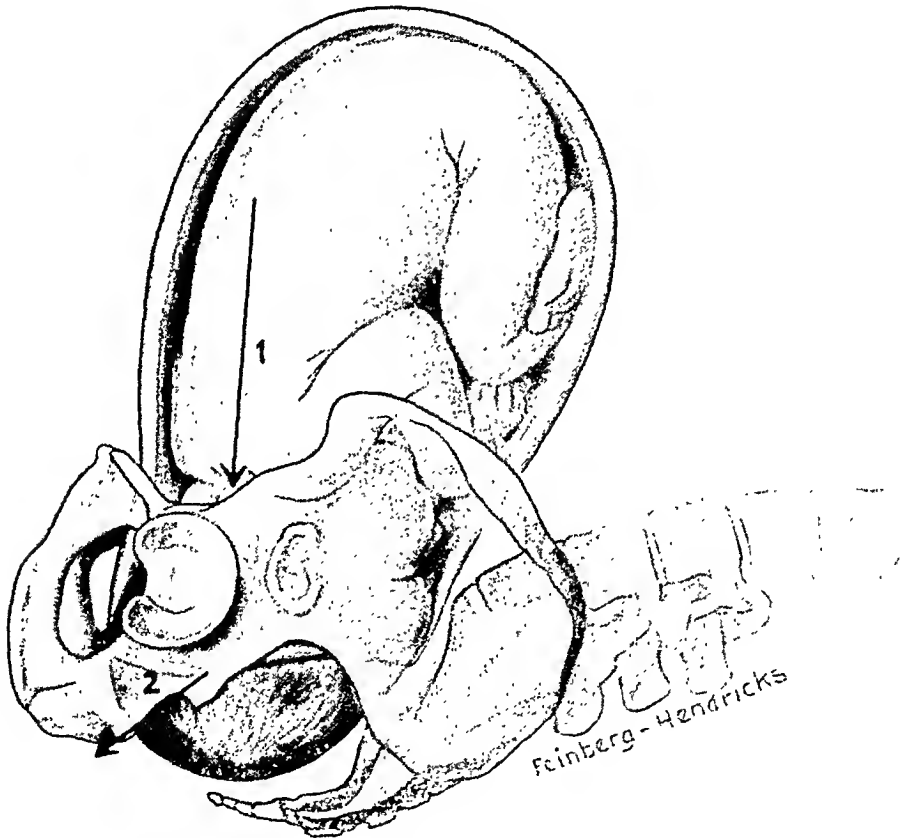


Fig. 29.—Normal mechanism of labor. Anterior position: descent to bottom of posterior pelvis to a region confined by forward sacral tip and coccyx in midline and the ischial spines laterally (the three-point landing). The head tends to be posterior to the perpendicular line from the inlet and avoids the lower fore pelvis.

Finally, the head descends to the lowest level of the fore pelvis until obstructed by the muscular pelvic floor alone, the flexed head angulated so that the chin occupies a high level in the posterior pelvis, with the anterior fontanel opposite the sacral tip. The long axis of the fetus is now oblique to the true pelvis, because the shoulders have moved forward close to the posterior aspect of the symphysis. The occiput at the height of a contraction passes at an angle downward, partially through the subpubic arch, before any act of extension begins. In fact, the head, as Hodge<sup>4</sup> and others have noted, descends

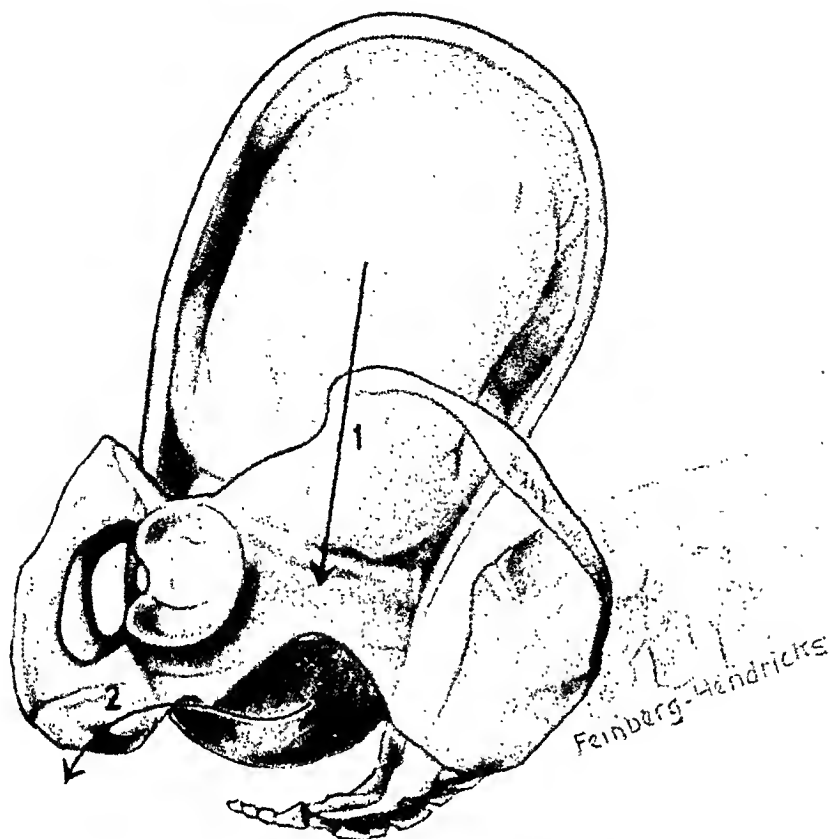


Fig. 30.—Normal mechanism of labor. Transverse position: descent to bottom of posterior pelvis to a region confined by forward sacral tip and coccyx in midline and the ischial spines laterally (the three-point landing). The head tends to be posterior to the perpendicular line from the inlet and avoids the lower fore pelvis.

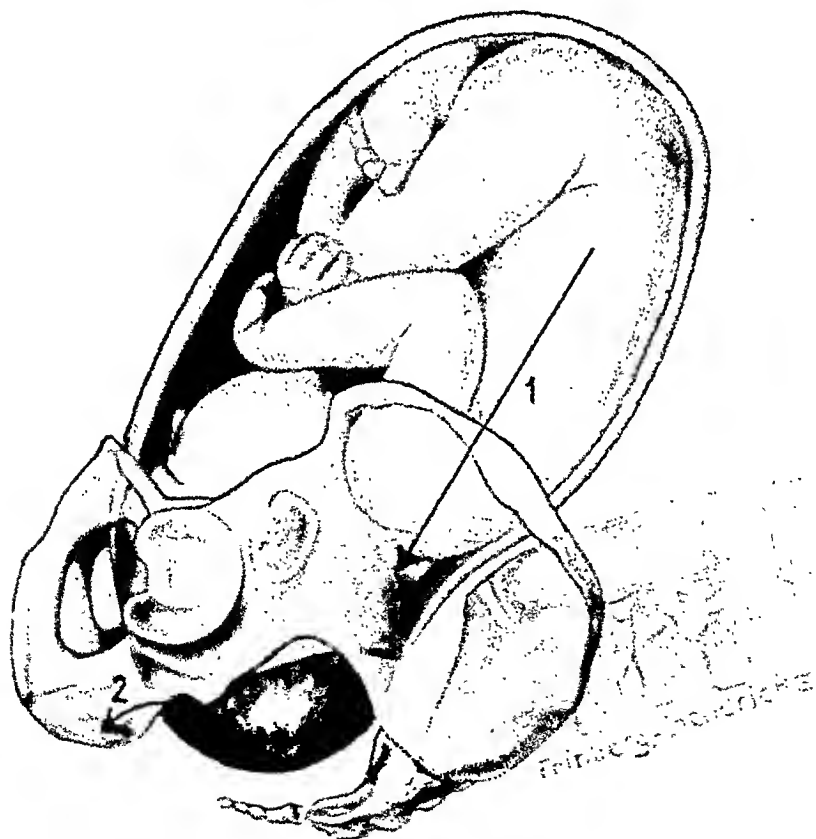


Fig. 31.—Normal mechanism of labor. Posterior position: descent to bottom of posterior pelvis to a region confined by forward sacral tip and coccyx in midline and the ischial spines laterally (the three-point landing). The head tends to be posterior to the perpendicular line from the inlet and avoids the lower fore pelvis.

until the biparietal diameter is opposite the intertuberos diameter of the pelvis before the act of extension begins, Fig. 33. The base of the occiput and the neck of the child are on a level with the under surface of the symphysis. This low descent of the head before extension occurs is not generally appreciated, nor is the fact that coincident with this, the occiput, descending in the axis of the fore pelvis, has partially passed through the subpubic arch, Fig. 36.

Note the attitude of the fetus illustrated in Fig. 36. This attitude allows a maintenance of flexion and at the same time permits the caput to descend downward and forward partially through the subpubic arch. The greater the angle between the plane of the symphysis

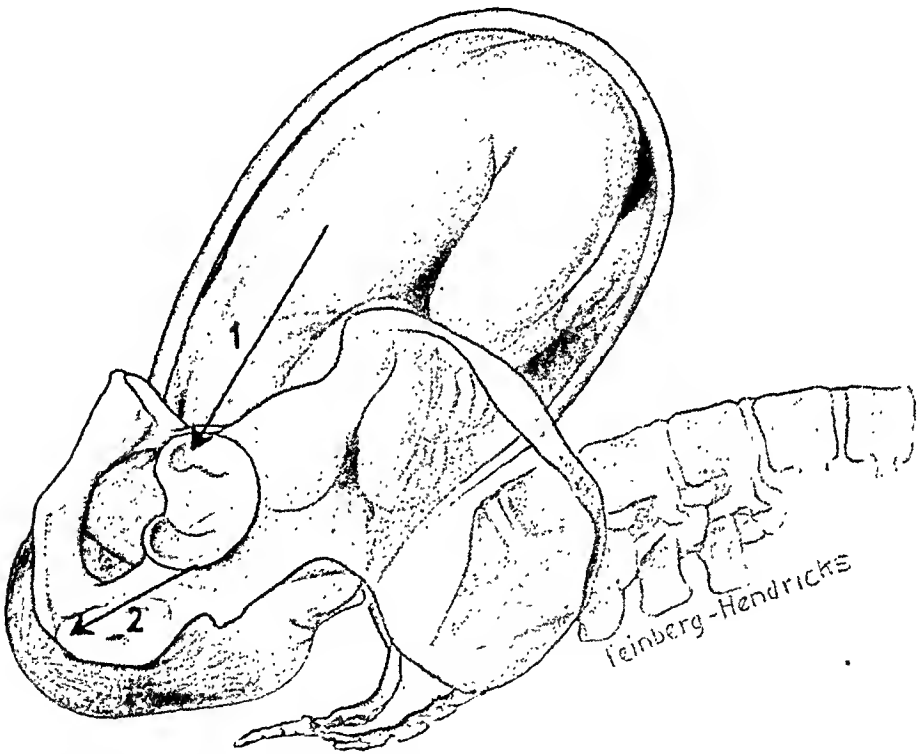


Fig. 32.—Normal mechanism of labor. Rotation to anterior position. Back close to symphysis. With a contraction, fetus descends against perineum in axis of fore pelvis (see Fig. 24, G, F. of E. F.).

and the plane of the pubic rami, the more significant this angular passage of the occiput through the arch becomes, in view of the fact that the head is virtually free of the confines of the bony pelvis before the sudden act of extension begins. The act of extension primarily is caused by the strong transverse muscles between the lower aspects of the ischiopubic rami. As the head swings forward, free of the tuberosities of the ischium, the shape of the dilating gutter creates a curved axis which carries the occiput in front of the plane of the symphysis, while only the neck of the child is brought in contact directly below the symphysis with the subpubic ligament and the upper portions of the pubic rami, Fig. 37.

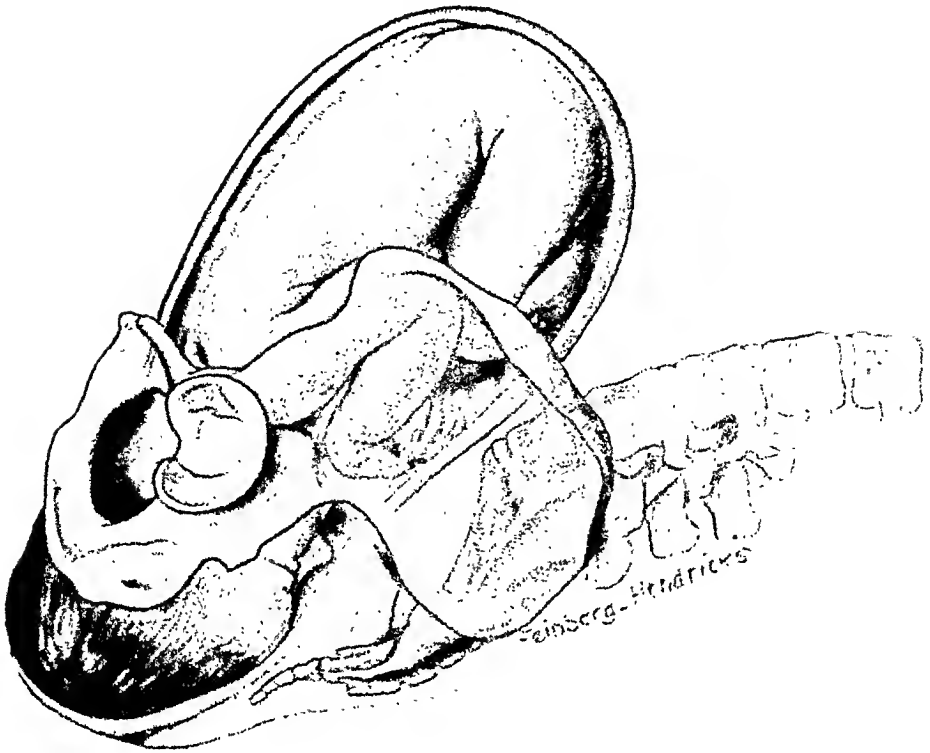


Fig. 33.—Normal mechanism of labor. Anterior position. Vertex descending to low level with biparietal diameter in the intertuberosus diameter. Perineum bulging. Flexion maintained. Neck of fetus behind under-edge of symphysis.

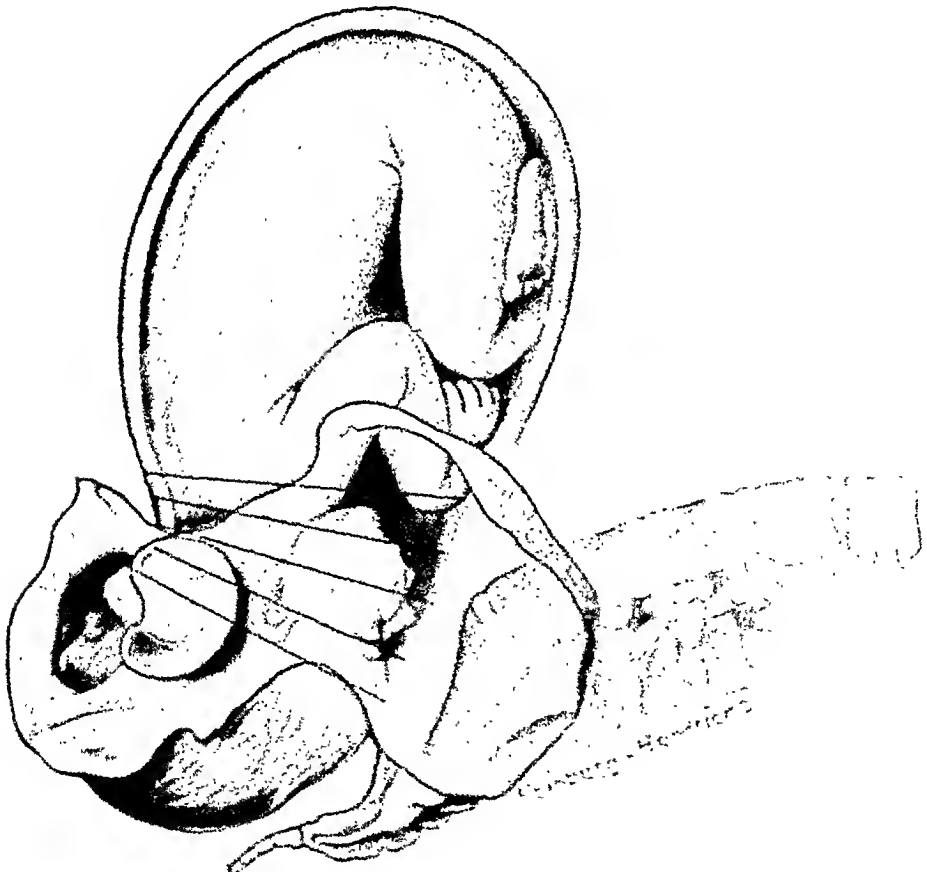


Fig. 34.—Between contractions the fetal attitude shown in Fig. 32 may reveal the attitude illustrated above, since the tense lower uterine soft parts attempt to hold the fetal body close to the posterior wall of the pelvis.

The manner by which the shoulders become adjusted to the shape of the pelvis is difficult to study. The stereoroentgenograms reveal the child at rest between contractions, and under these conditions it is unusual to observe any obvious twist at the neck, irrespective of the position of the head. After the vertex is born, the shoulders, descending into the pelvic cavity, rotate, and the head follows in the so-called act of restitution. Further work is necessary to clarify ideas on the factors concerned in restitution.

A clear understanding of this mechanism will explain why the handles of the forceps must not be elevated until the caput is well

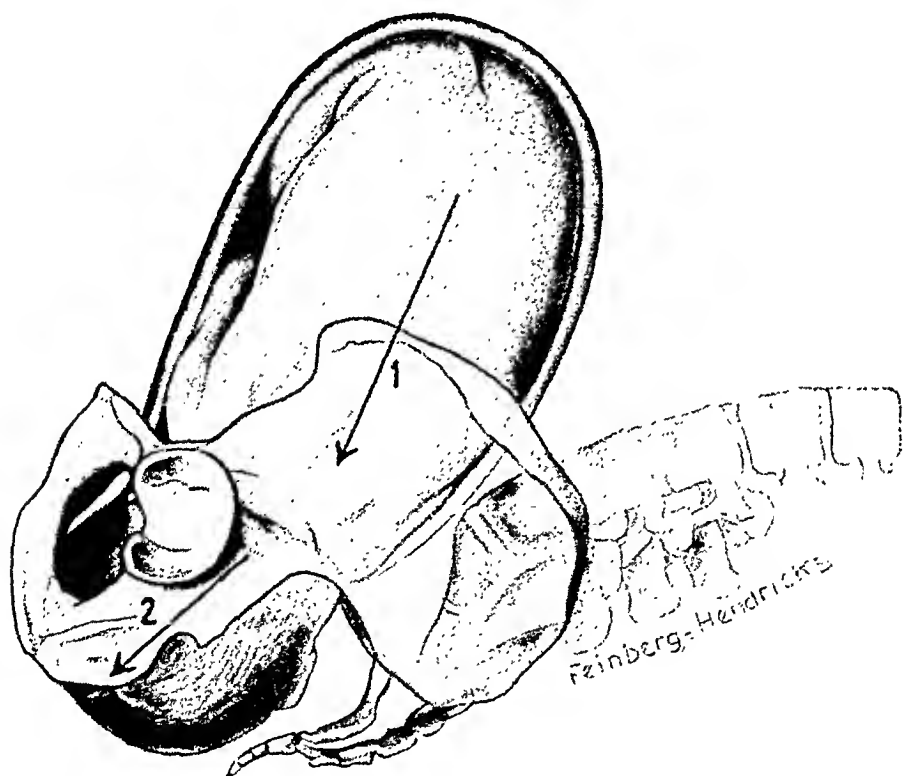


Fig. 35.—Normal mechanism of labor. If rotation fails to occur at level shown in Fig. 30, a transverse position descending into fore pelvis must demonstrate "anterior lateral flexion." This movement occurs characteristically in android types.

showing. Traction must be made in the axis of the fore pelvis to cause the head to descend downward and forward, partially through the subpubic arch, before the act of extension is encouraged.

In the course of our study of this normal mechanism, we had occasion to study certain deviations from it which we will discuss briefly. We hope that in subsequent publication we will be able to point out other deviations of equal importance.

#### 6A. MECHANISM IN THE ANDROID AND FLAT Pelves

In a recent report we have shown that in normal pelves engagement occurs in 70 per cent of the cases in the transverse position.<sup>3</sup> But most

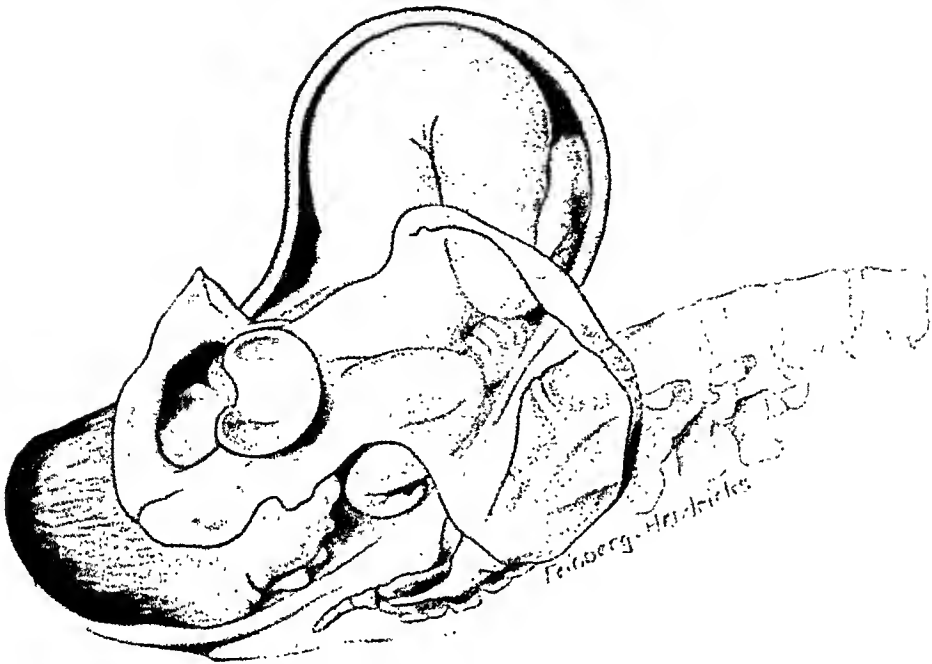


FIG. 36.—Flexion frequently is maintained even as the head begins to pass downward through the subpubic arch. This necessitates a peculiar attitude of the fetus with arching of the back, as illustrated.

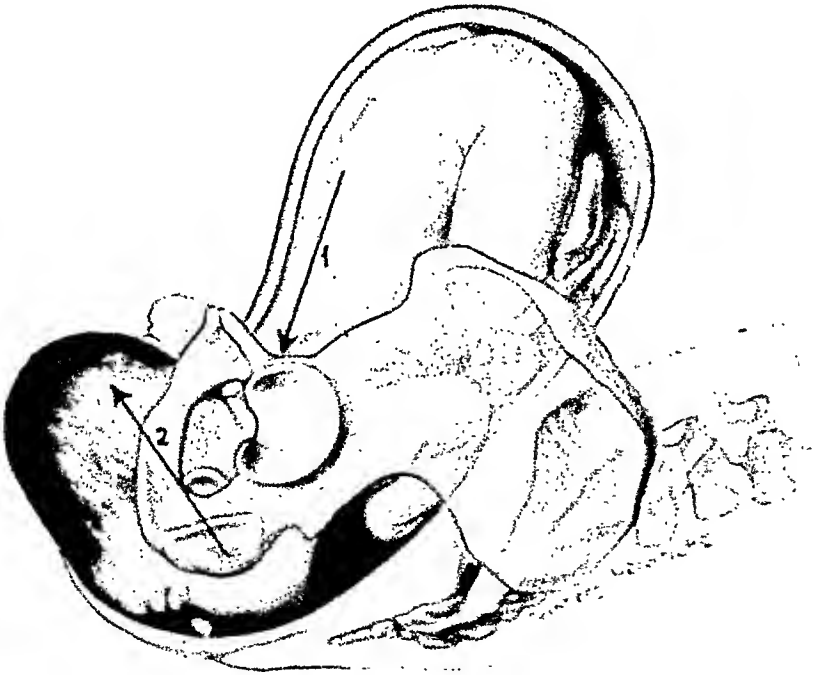


FIG. 37.—As the head is grasped by Ritzen's manoeuvre, extension begins rapidly. The head, already partially through the subpubic arch, extends rapidly and is directed upward in axis of soft part canal in this region to clear the transverse muscles of the pelvic diaphragm. The lower occipital region and neck of the child utilize the upper aspects of arch under symphysis.

obstetric authorities associate "deep transverse arrest of the head" with the posterior position, in that it is assumed to represent an incomplete stage in the process of anterior rotation. Our statistical evidence from the large series of case studies, which we have as yet made no attempt to tabulate, definitely associates this condition with the android pelvis, in which the mechanism is that of a transverse position from the inlet to the level of arrest. It is the exception rather than the rule to find a posterior position at higher levels in the pelvis in a case which becomes arrested in the transverse position lower in the pelvis. Occasionally, at higher levels in this type of case, the transversely placed median sagittal suture may be slightly anterior or posterior to the exact transverse plane, but not sufficiently obvious to warrant classing the position as other than a transverse.

The high incidence of characteristic android forms in the cesarean section and midforceps group of this series warrants considering the android pelvis as potentially the cause of more serious obstetric difficulty than any other single pelvic type. The problem is rendered more serious when it is realized that android pelvises are prone to occur in rather characteristic physical types, which are poor subjects for labor. The child is usually above average weight and may display, in addition, definite evidence of postmaturity. We have consistently observed that, when a large head delivers normally through an abnormal pelvis, the mechanism of labor has been so directed by efficient uterine contractions and normal reacting soft parts as to allow the maximum in fetal pelvic adaptation for all levels of the pelvis, according to the principles discussed in normal labor. This indicates that difficulty in labor is not simply one of head size *versus* pelvic size, but that the behavior of the uterus and of the soft parts is a most important factor. This accounts for the observation made by us over and over again that, with the same size of head and the same type and degree of pelvic abnormality, one patient may deliver spontaneously while another requires a forceps delivery or even a cesarean section. Thus any facts concerning the peculiarities of the mechanism of labor in android types become especially important.

The narrow sacrospinous notch, associated with the short, posterior iliac portion of the inlet over the apex of the notch, and with the sharp inward curvature of the posterior extremity of the iliopectineal lines, is characteristic of the typical android posterior pelvic segment. The shape of the lateral extremities of this flat posterior segment does not favor engagement of the occiput in the oblique position, unless the fore pelvis is sufficiently long and narrow to introduce an anthropoid tendency. In this latter event, engagement in the oblique posterior position will be favored.

Accordingly, in the more typical android types, engagement can occur only in the transverse position. A posterior parietal tendency usually is present at the inlet, but with reasonably efficient labor the anterior parietal bone descends more rapidly than the posterior, and the fetal head becomes directed into the posterior pelvis close to the sacrum.

Normally, in gynecoid or more ample pelvic types, spiral anterior rotation begins when the head has reached the bottom of the posterior pelvis.

In android forms, however, rotation is prevented at this level by the shape of the pelvis at the inlet, and hence the head must descend to a much lower level for rotation to occur. In Figs. 38 to 41, the anatomical explanation for the persistence of this occipitotransverse position, and for the mechanism which obtains in the lower pelvis, is illustrated. It will be observed that the temporal region of the partially flexed head meets with the resistance of the lateral aspects of the sacral alae at the inlet as soon as there is any attempt at rotation at or above the ischial spines (Fig. 38). This influence continues to act even when the head has descended to a low level in the posterior pelvis, Figs. 39 and 40. In Fig. 39 a lateral view shows the vertex close to the sacrum, with the median sagittal suture of the head in the region of the interspinous diameter. The resistance offered by the lower curved surface of the terminal sacrum and coccyx, along with the sacrospinous ligaments originating laterally from the ischial spines, prevents further descent in the axis of the posterior pelvis. Since rotation cannot occur, due to the reason suggested above, and descent must continue, the median sagittal suture moves forward and downward into the fore pelvis under the influence of straight drives along the fetal axis with each uterine contraction (Fig. 40). Between contractions the head demonstrates "anterior lateral flexion" in relation to the fetal body, so that this movement into the fore pelvis may be termed "anterior lateral flexion," Fig. 40. This movement occurs in normal labor synchronous with rotation and descent on the pelvic floor. But, in android pelvises, sufficient descent must be gained to allow the brow to sweep under the promontory, and only when this act is mechanically possible can rotation take place, Fig. 41. It is possible, though rare in occurrence, for the head to be delivered in the O T position by a movement of extreme anterior lateral flexion.

The above description of the mechanism of labor may be considered normal for the android type and is that which occurs in physiologic labor in these cases. Naturally, if this premise is correct, it is important, when forceps are used for "deep transverse arrest of the head,"



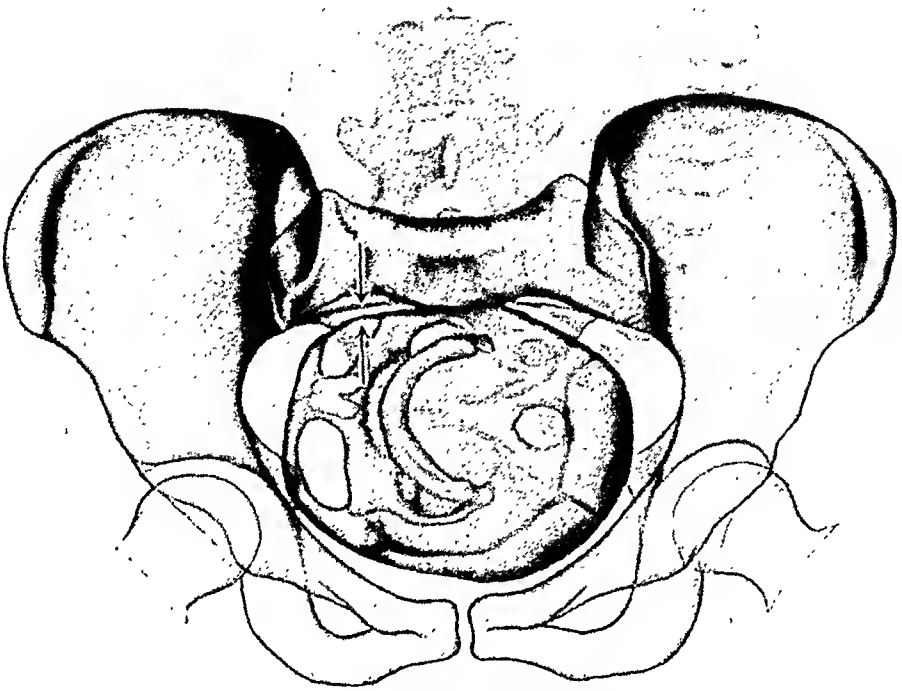


Fig. 38.—The normal mechanism in android types (occiputotransverse position maintained to a low level). Inlet view: rotation from the O T position to an oblique anterior position fails to occur in the low posterior pelvis on account of the opposing forces between the temporal region of the head and the lateral aspects of the sacral region at the inlet (see arrows).

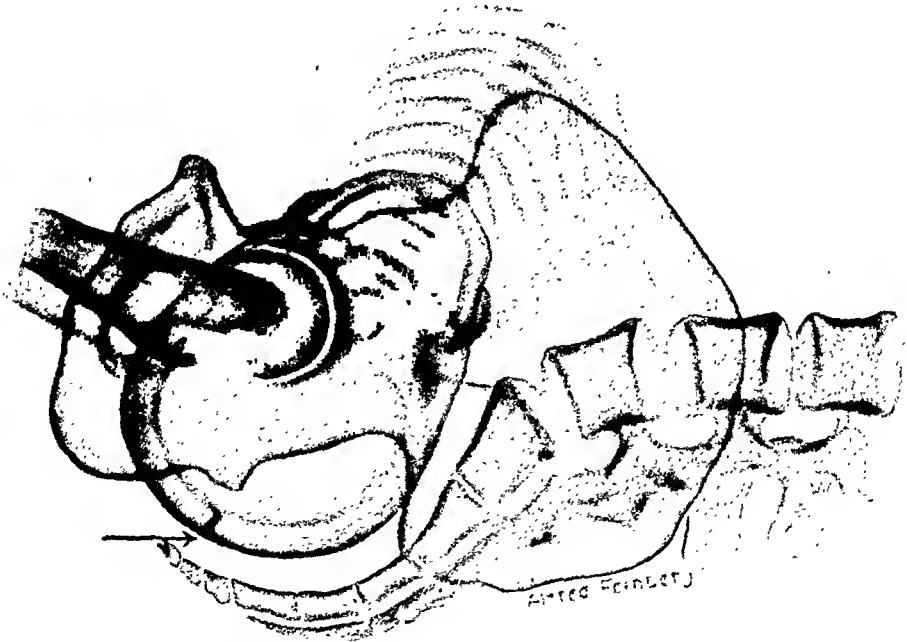


Fig. 39.—Normal mechanism in android types. Lateral view of Fig. 38. Vertex in O T position at bottom of posterior pelvis close to lower sacral region.



Fig. 40.—Normal position in android types. Lateral view. If the side walls of the pelvis are sufficiently wide, the O.T. position persists (for reasons given in g. 38). For descent to occur the head demonstrates "anterior lateral flexion" between contractions as it descends in the fore pelvis. This means that the median sagittal suture moves more and more in front of the ischial spines and downward.

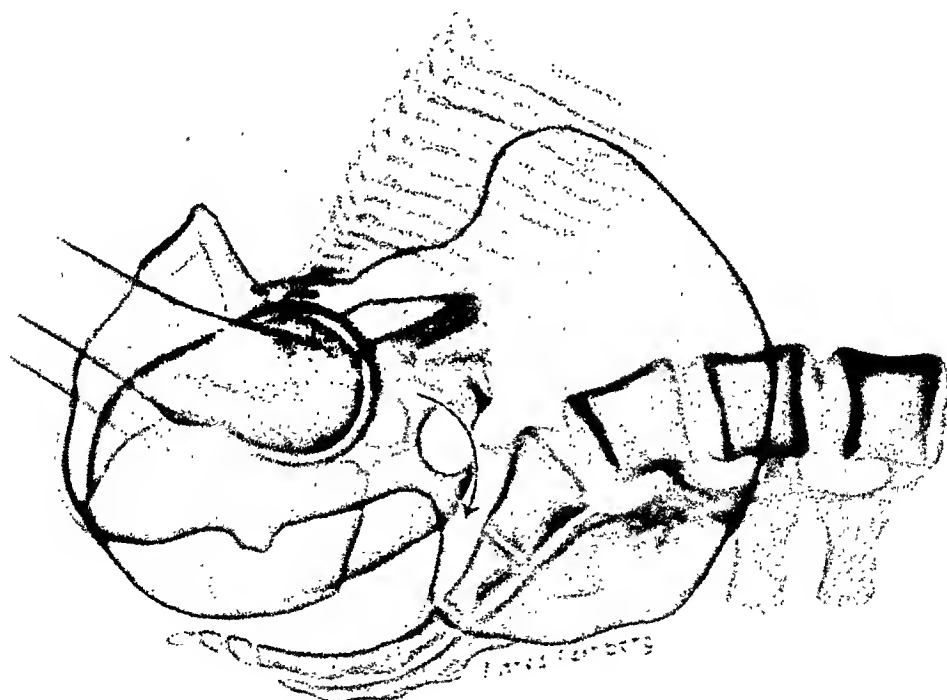


Fig. 41.—Normal mechanism in android types. Lateral view. Anterior spiral rotation from the O.T. position occurs at such a level in the lower fore pelvis that the fetal brow may move without resistance under the promontory.

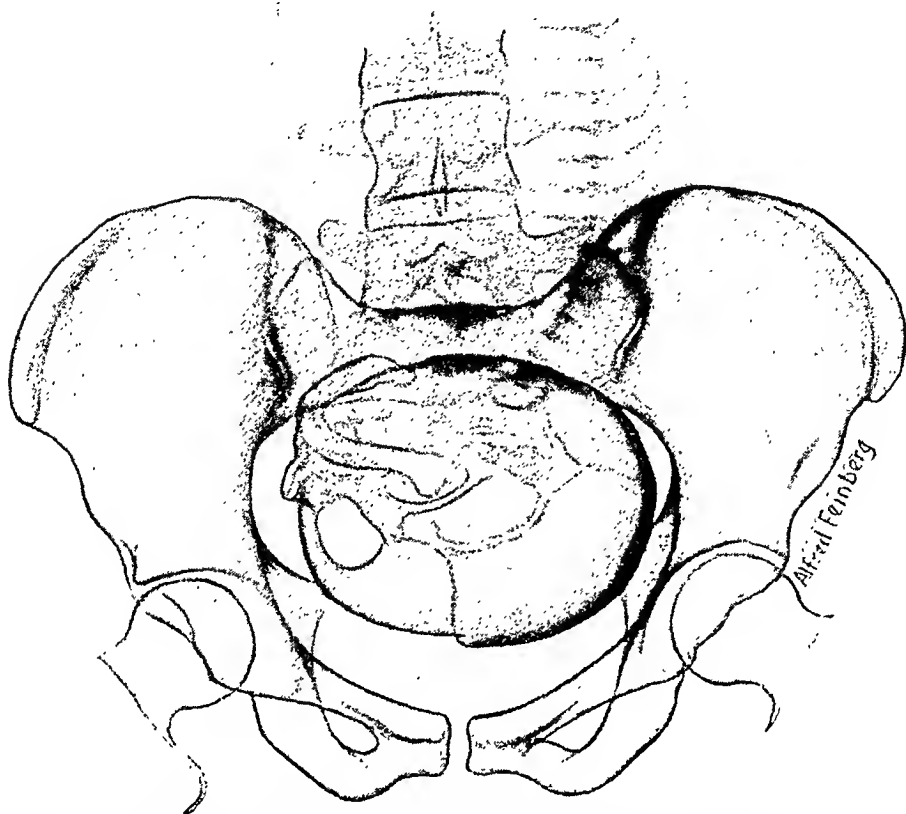


Fig. 42.—The mechanism of labor in android pelvis, as complicated by a narrow interspinous diameter. Normal posterior parietal O T position engaging at inlet.

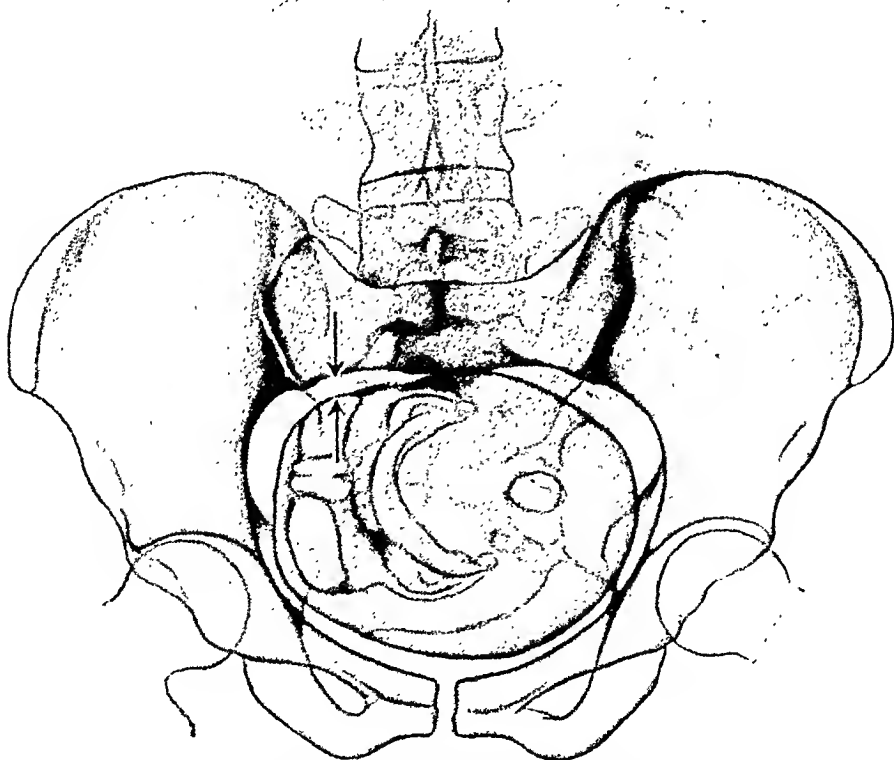


Fig. 43.—Same case as Fig. 42. Arrest at bottom of posterior pelvis in the O T position. Rotation to anterior oblique position is prevented by the flat android pelvis at the inlet (see arrows) and the narrow interspinous diameter below.

to maintain this O T position until the head has been brought to the proper level at which rotation can occur. We have a number of cases where this principle with forceps has not been applied, and too early attempt at rotation of a poorly flexed and unmolded head have resulted in stillbirth or serious soft part injury to mother and child.

If the O T position is maintained, descent can occur only if the side walls are straight and the intertuberosus and interspinous diameters are wide. This point is important. The presence of a narrow interspinous diameter greatly complicates the problem of rotation and descent of the transverse position, as illustrated in Figs. 42 and 43.

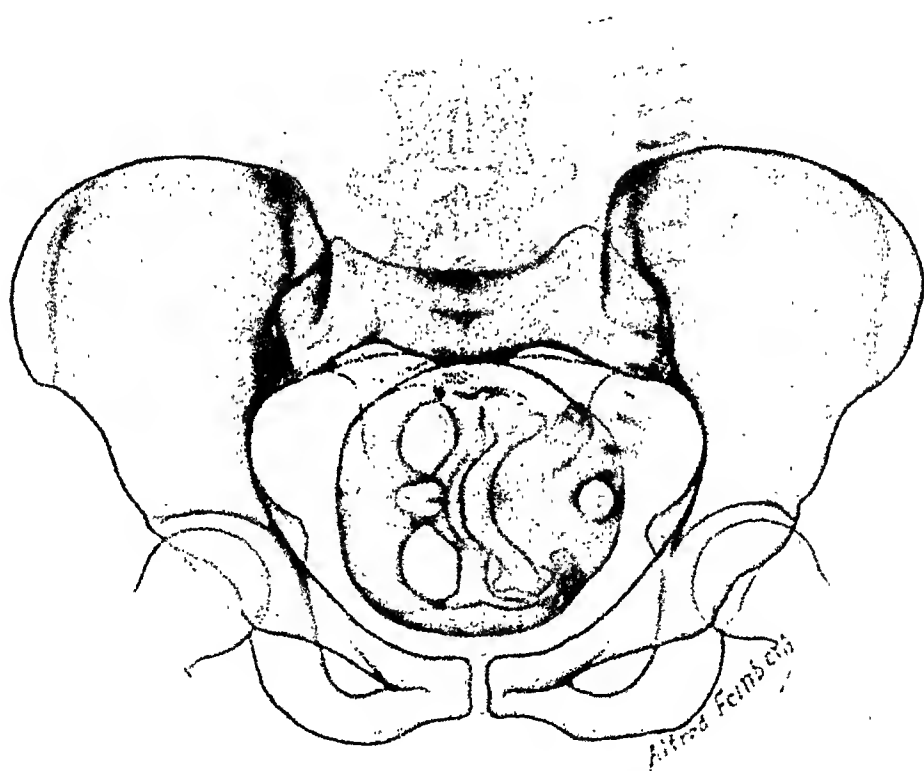


FIG. 41.—When a head is well flexed, rotation is usually accomplished by manual methods in any type of pelvis (android type illustrated).

In fact, this type of pelvis may offer one of the most difficult problems in obstetrics from the mechanical standpoint. Unless the obstetrician is cognizant of the narrow interspinous diameter and the android character of the posterior pelvis, and is aware of the fact that these two abnormalities are acting to prevent rotation and descent, traction by forceps is likely to be misdirected, and version and breech extraction may in the end be the safer method of delivery. In the case illustrated, Figs. 42 and 43, the poorly flexed head could not be rotated because the temporal region conflicted with the lateral alae of the sacrum at the inlet, while, below, the narrow interspinous diameter offered obstruction to the forward rotation of the occiput. In other words, the head could not descend below the posterior pelvis

in the O T position to utilize the fore pelvis. No great difficulty had occurred up to this point, the head having engaged in a posterior parietal position, as illustrated in Fig. 42. The cervix was almost fully dilated. The case was handled as follows: Barton forceps were easily applied after it had been demonstrated that manual rotation of the head to the anterior oblique position could not be performed. With traction, the head was brought down as close as possible to the level of the lower sacrum and ischial spines, at which point a lateral laceration of the vaginal wall occurred adjacent to the left ischial spine. With gentle traction, the head became better flexed and, on removing the forceps, it was possible to rotate the head manually to an oblique anterior position, *because a well-flexed head can rotate in any type of pelvis*, Fig. 44. After this degree of rotation had been obtained, the delivery was easily accomplished by the use of Haig-Ferguson forceps, the head slowly rotating in a spiral manner to an anterior position. The lateral laceration of the vagina increased in extent as the head approached the outlet.

#### 6B. FETAL PELVIC ADAPTATION

The position in which the head lies before or at the onset of labor is not necessarily determined by the shape of the pelvis, unless the head is already deeply engaged at that time. When the head is not deeply engaged, certain factors in the soft parts, which cannot always be determined in the individual case, influence the position. Such factors may be the shape or obliquity of the uterus, the position of the placenta, or even the length of the cord.

Thus we find posterior positions occurring in normal pelvises and, with the onset of labor, descending in this position, according to the normal mechanism, to rotate spontaneously in the muscular gutter of the outlet. In certain pelvic types, however, engagement of the head in the position originally present at the inlet would result in arrest before engagement could be effected, unless adaptation to a more suitable position occurred. Representative examples are illustrated in Figs. 45 to 48. In Fig. 45 an original oblique posterior position rotated to a transverse position (Fig. 46) as engagement occurred. Such adaptation is necessary in this platypelloid (flat) pelvis or in the android type with a flat tendency. In Figs. 47 and 48, the pelvis conforms to a fairly typical anthropoid type with a narrow fore pelvis. An original anterior oblique position was maintained, without descent, until membranes ruptured with cervix fully dilated, at which time the vertex spiraled posteriorly to an oblique posterior position and descended into the low posterior pelvis. The rounded occiput avoids a narrow fore pelvis, and this necessitates engagement in the posterior position if the anteroposterior diameters

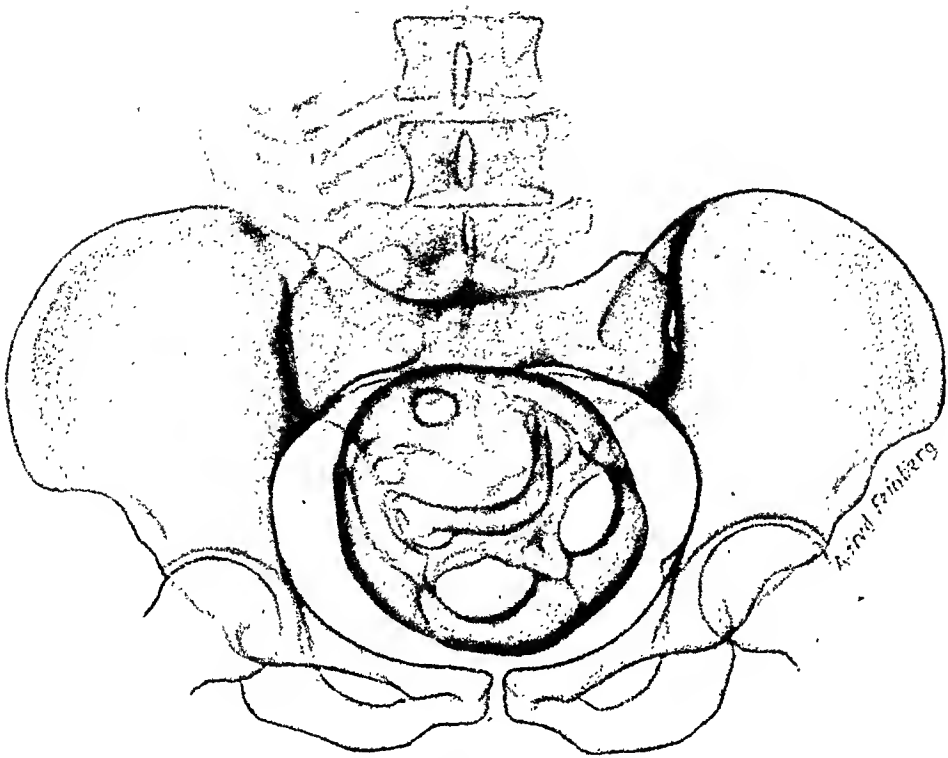


Fig. 45.—Fetal pelvic adaptation at the inlet. An original posterior position in a flat type of pelvis. This position is caused by the soft parts.

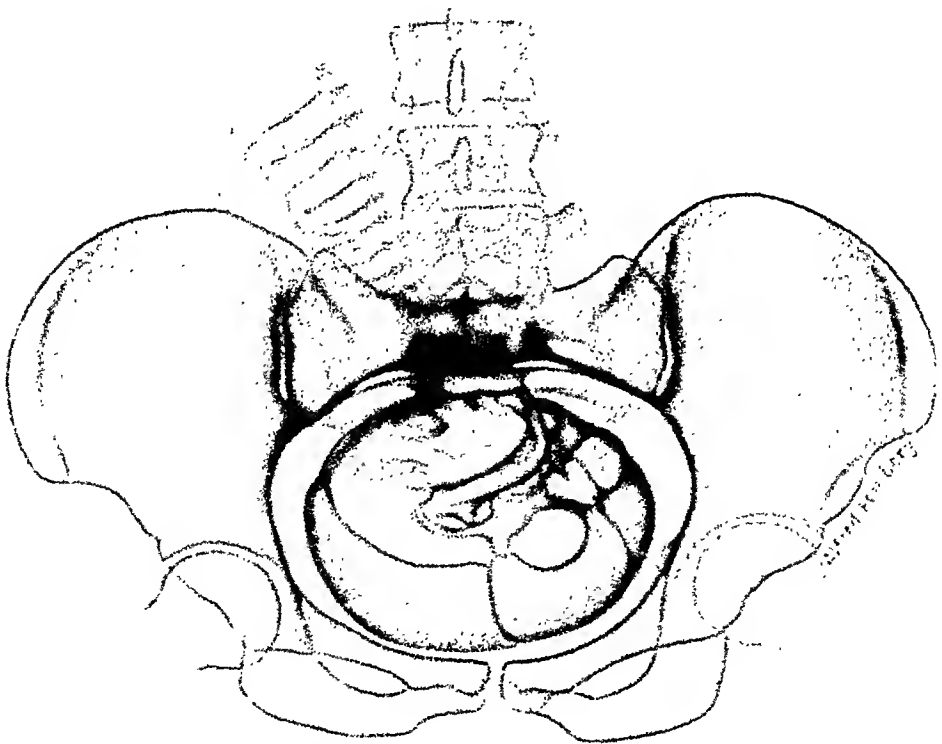


Fig. 46.—Fetal pelvic adaptation at the inlet. Same case as Fig. 45. For engagement to occur the head must adjust itself to the inlet to a transverse position. This latter position is maintained to a low level for reasons illustrated in Figs. 28 to 41.

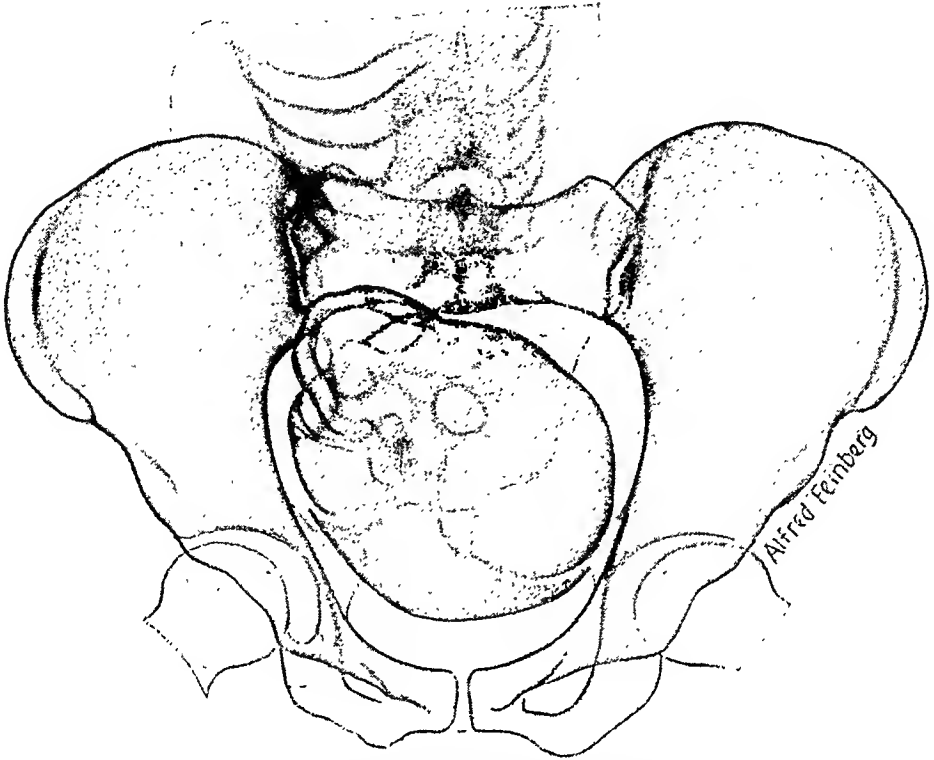


FIG. 47.—Fetal pelvic adaptation at the inlet. An anterior oblique position at the inlet in an anthropoid type with a narrow fore pelvis.



FIG. 48.—Fetal pelvic adaptation at the inlet. Same case as FIG. 47. The head, remaining high until membranes ruptured, engaged and rotated in a spiral manner to an oblique posterior position. The occiput is not as adaptable to a narrow fore pelvis as is the frontal aspect of the head.

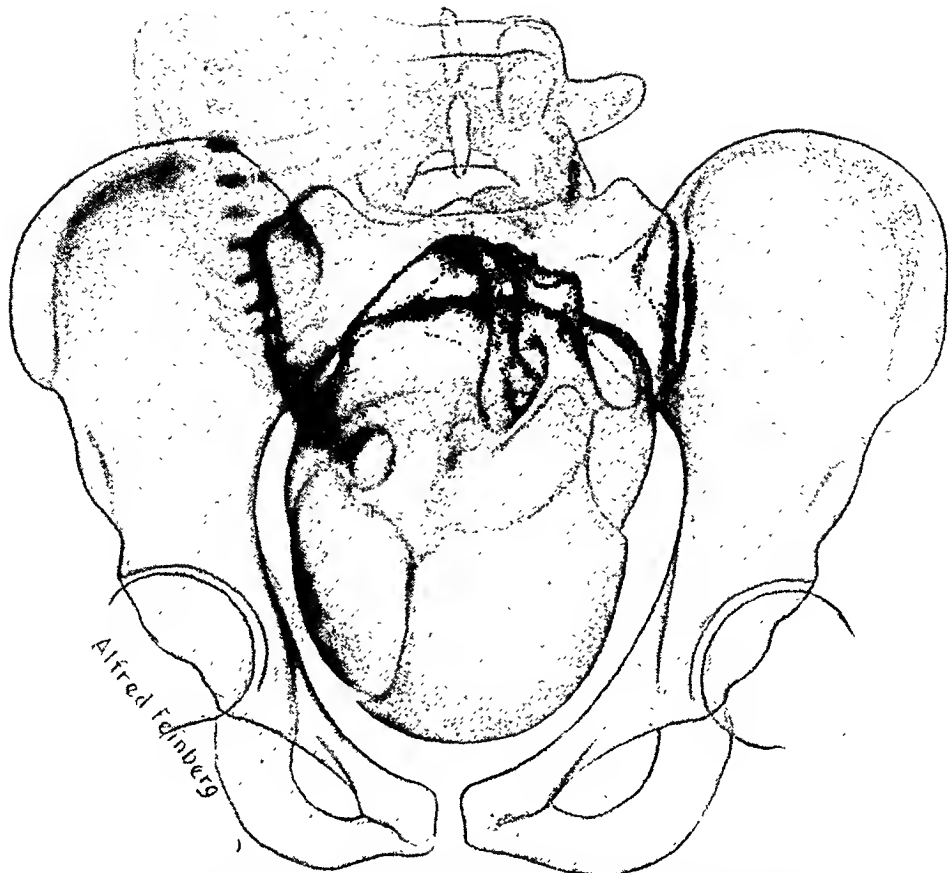


Fig. 49.—Abnormalities in the mechanism of labor at the inlet. Arrest of an anterior oblique position in an anthropoid type with a narrow fore pelvis. Appearance of the head (inlet view) wedged in the narrow fore pelvis in an oblique anterior position.

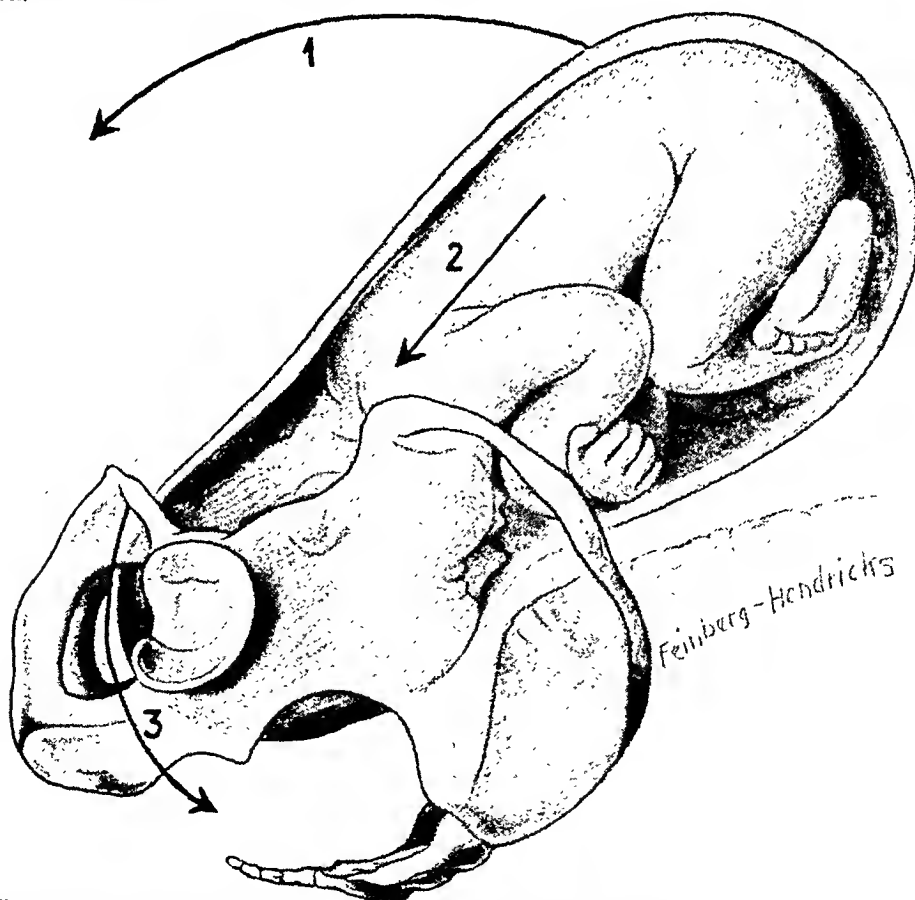


Fig. 50.—Diagrammatic illustration of the same case (Fig. 49) from the lateral aspect. The head is impacted in the narrow fore pelvis. Thus the uterus is prevented from swinging forward, and the head cannot move downward and backward to utilize the available posterior pelvis as in the normal mechanism of labor.



are long, as in the anthropoid type. In certain pelvises with a narrow fore pelvis and a wide posterior pelvis, as in the android type, engagement will occur in the transverse position in order to avoid the narrow angle in the anterior part of the inlet. If considerable narrowing exists in the transverse diameter posteriorly, the head may not be able to enter even in the posterior position. Under these conditions, the head is forced to descend into the fore pelvis in an anterior position, as illustrated in Figs. 49 and 50. The head, in this case, descended obliquely downward and forward and finally arrested in the upper midpelvis, becoming wedged in the narrow fore pelvis. The uterus and fetal axis could not swing forward to make the head descend posteriorly toward the sacrum, as in the normal mechanism of labor. A difficult forceps delivery, resulting in a stillbirth, occurred, and it was mechanically difficult to direct the head downward and backward to make it utilize the posterior pelvis, as it does in normal labor. Traction virtually was made down through the fore pelvis before either the pubic or sacral segment of the soft parts had dilated and retracted. In this case, version and breech extraction would have allowed the head to utilize the posterior pelvis to better mechanical advantage.

#### 6C. THE TYPE OF PELVIS ASSOCIATED WITH THE PERSISTENT POSTERIOR POSITION

Considering the volume of literature which has accumulated during recent years on the posterior position, it would seem that very little remains to be discussed concerning etiology or treatment of this obstetric problem. DeLee,<sup>11</sup> for instance, has accurately described the peculiar pelvic canal commonly found in persistent posterior positions, while the importance of the narrow interspinous diameter has long been recognized. At this time, space permits only brief discussion of the particular type of pelvis commonly associated with a persistent posterior position, and the type of pelvic canal which may permit either an efficient or inefficient uterine drive into the pelvic cavity through the fetus.

In Figs. 51 and 52 a posterior position is illustrated which has descended to a low level, with caput showing. At the time the roentgenograms were obtained, from which these diagrams were constructed. Presumably, the head, in spite of the shape of the pelvis, has descended through the pelvis according to the principles described above for the normal mechanism of labor. In all likelihood, the patient would eventually have delivered in a persistent posterior position if the condition had not been recognized. The pelvis in this case conforms to the android type with an anthropoid tendency. In other words, it possessed a long narrow fore pelvis, which insures a long

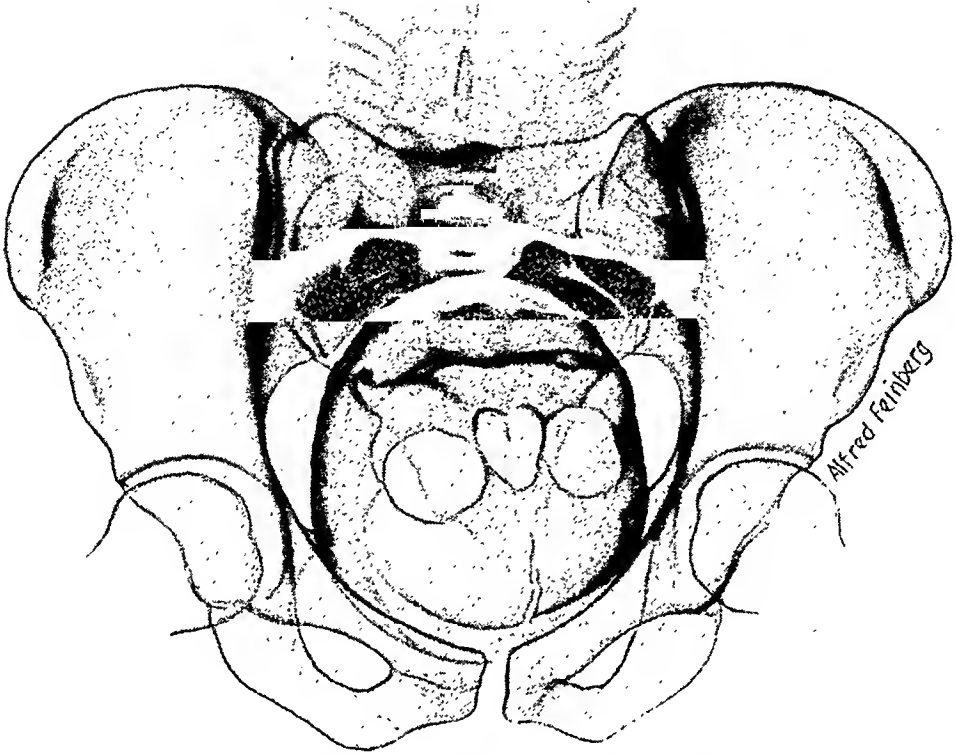


Fig. 51.—The type of pelvis associated with the persistent posterior position. The persistent direct O P position low in the fore pelvis (inlet view). The pelvis conforms to the *android* type with *anthropoid* characteristics, converging side walls, and possesses a narrow interspinous diameter.

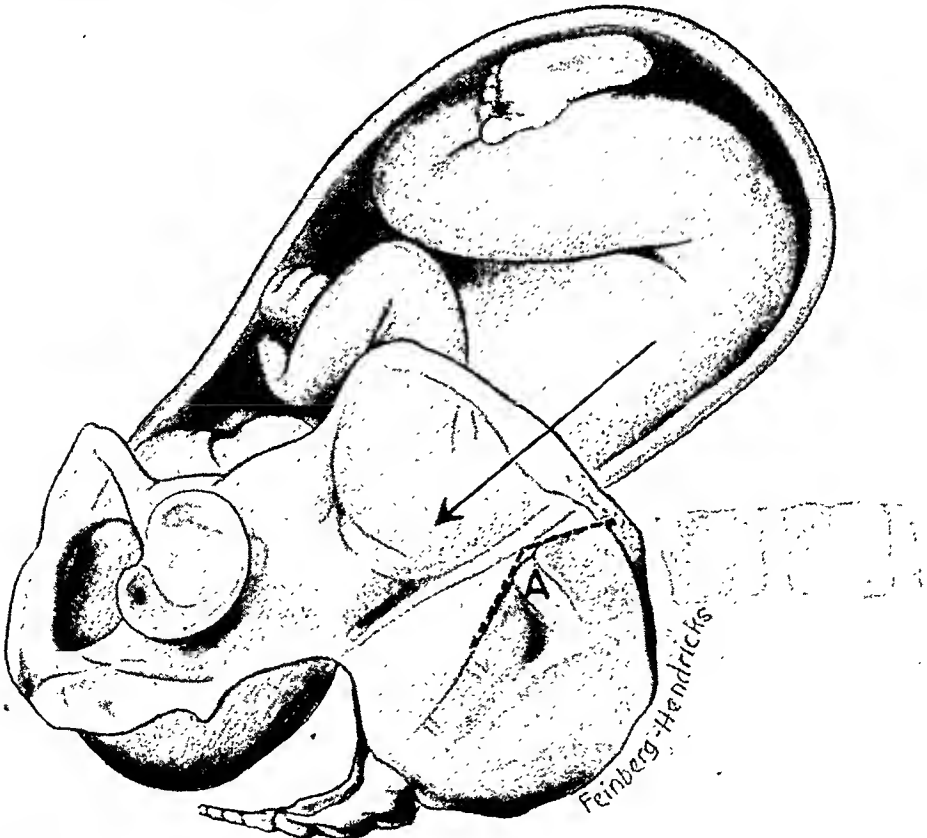


Fig. 52.—Same case as Fig. 51 from the lateral aspect. The normal mechanism of labor has been followed, and descent has occurred to a low level, largely, we believe, because the uterine contraction has been enabled to exert its influence as a straight drive through the fetus because of the wide angle at "A."

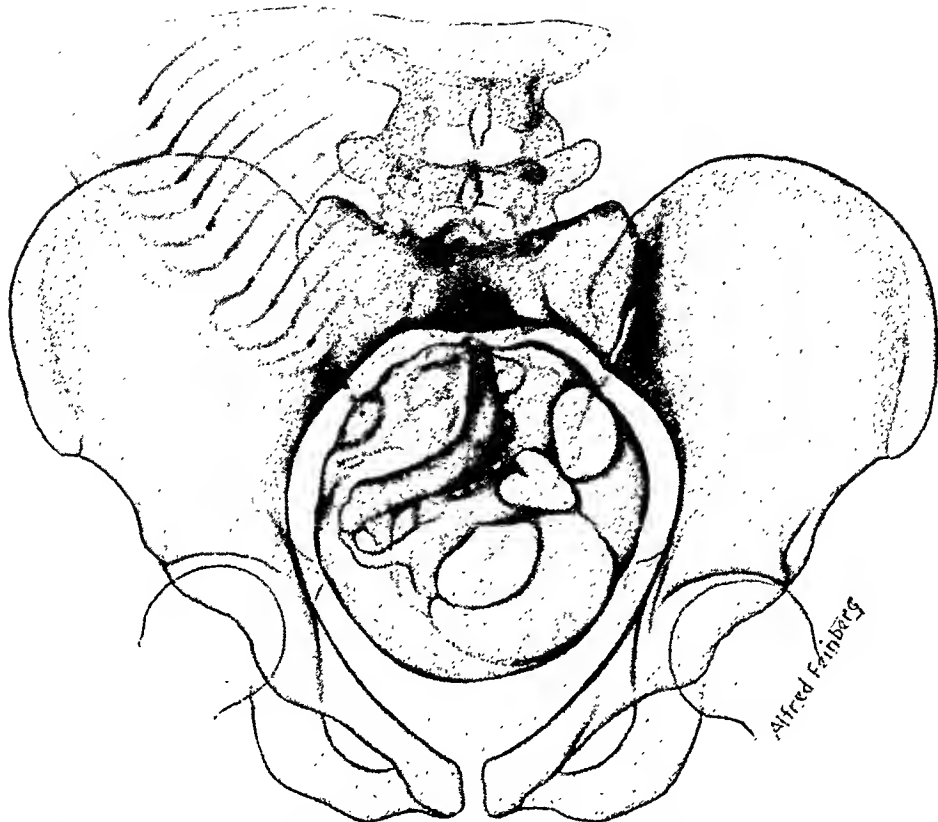


Fig. 53.—The type of pelvis associated with a persistent posterior position. Arrest of the head at bottom of posterior pelvis in the oblique O P position. The pelvis conforms to the *typical anthropoid type with straight side walls and a moderate outlet*. The fore pelvis is avoided. The head is impacted close to the sacrum and side walls of the pelvis.

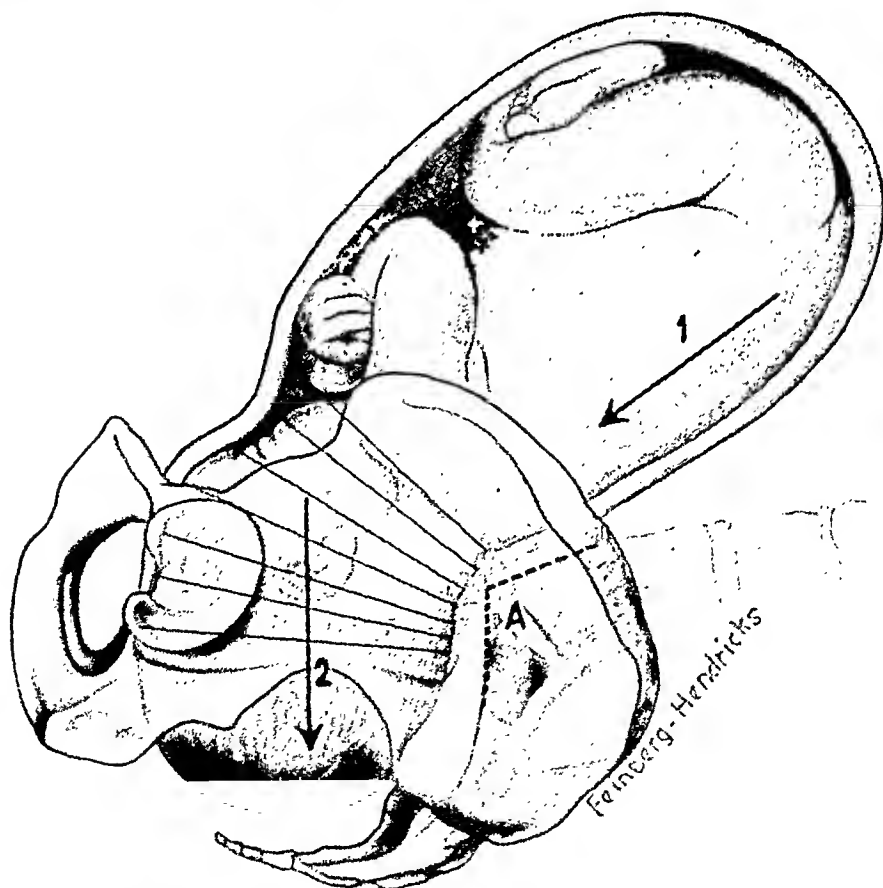


Fig. 54.—Lateral view of same case as Fig. 53. Tense soft parts hold head against sacrum. The sharp angle at "A" prevents the uterus from gaining a direct drive through the fetal piston into the posterior aspects of the pelvis. Note the posterior angle between axis of fetal body (1) and head (2).

anteroposterior diameter in spite of the android posterior pelvis. The side walls of the pelvis, in addition, converge toward a moderately narrow subpubic angle, causing noticeable narrowing of the interspinous diameter. These facts undoubtedly introduced sufficient resistance to the head to prevent rotation after descending through the pelvis in the oblique posterior position. The lateral view shown in Fig. 52 helps to explain the reason for this low and rapid descent. Notice that the lumbosacral angle at "A" is wide, so that the uterine drive in the fetal axis was efficient. In all probability, if the pelvis were more oblique to the vertebral column, as in Fig. 54, arrest would have occurred at a higher level. In this case, the well-flexed and well-molded head was easily rotated manually after the impaction was relieved by elevation of the head.

A posterior position which required forceps delivery is illustrated in Figs. 53 and 54. The pelvis conforms to a large anthropoid type with a definitely narrow transverse diameter throughout the pelvis, but with straight lateral walls and a moderate subpubic angle. The head became arrested at the level of the spines in the position shown in Fig. 53. Note that the head has descended, avoiding and not using the fore pelvis. It is situated so close to the sacrum and side walls, in the oblique posterior position, that attempts at manual and instrumental rotation were unsuccessful, due to the impacted condition. The cervix was almost completely dilated, but a thick, tough rim encircled the head. Forceps were finally applied pelvically with the head in the direct O P position and, with traction, the caput appeared. The lateral diagrammatic view of this case in Fig. 54 reveals an important factor in the lumbovertebral angle and the type of pelvic obliquity which we believed materially furthered the arrest. Note that the angle at "A" between the lumbar column and sacral surface is more acute than the example shown in Fig. 52. This anatomic arrangement predisposed to less flexibility at the lumbosacral joint, so that even with the lithotomy position the fetal axis could not be brought to bear directly downward into the posterior pelvis. In other words, the pelvis is more oblique to the vertebral column, and the fetus in its descent must "round" a sharp bend in order to descend through the pelvis. With the head at a higher level, the uterine drive, in spite of this abnormality, was sufficiently good to cause descent. Finally, as descent occurred, an increasing posterior angle between neck and body resulted. This prevented the transmission of the uterine force to the occiput, and contractions diminished in frequency and strength. Coincident with these results, the lower pole of the uterus became spastic, the rim of the cervix became edematous, and the descent finally ceased, with the head impacted and fixed against the lower sacrum, Fig. 54.

A roentgenogram, which illustrates to even better advantage the rôle normally played by the lower pole of the uterus in directing the head into the posterior pelvis and maintaining it close to the sacrum, is shown in Fig. 55. The pelvis conforms to the anthropoid type. The head, in the oblique posterior position, is not making use of the fore pelvis, but is located above and behind the ischial spines. In this example, spontaneous rotation of the posterior position occurred



Fig. 55.—A roentgenogram of an oblique posterior position which has descended to the midpelvis. The pelvis conforms to the anthropoid type. The lower pole of the uterus (outlined diagrammatically) directs the head into the more ample posterior pelvis above and behind the ischial spines, thereby avoiding the fore pelvis at higher levels. This principle concerning the rôle of the lower pole of the uterus applies to all pelvic types.

after the head had descended to the bottom of the posterior pelvis. A lateral roentgenogram of the same case revealed a pelvic canal similar in shape to Fig. 52.

Several examples of secondary posterior positions have been encountered which caused considerable difficulty in rotation in the lower

posterior pelvis. A representative case study is illustrated in Fig. 56. The pelvic type conforms to the gynecoid or normal type, but with the ischial spines protruding sharply inward to create a narrow interspinous diameter without affecting other transverse measurements in the pelvis. The head descended rapidly to the level of the spines, following the normal transverse mechanism (O T posterior parietal at inlet). At this point, the narrow interspinous diameter caused the occiput to rotate posteriorly and, as further descent occurred, the occiput became fixed behind the spine in the lower aspects of the sacrosciatic notch. Attempts at manual and instrumental rotation at that level were unsuccessful. Manual rotation was easily carried out after the head had been pushed up sufficiently to clear the ischial spines.



Fig. 56.—Arrest of the head in the O P position behind a narrow interspinous diameter, while the pelvis, generally, is quite ample. The head descended as a transverse position to the level of the spines and rotated to the oblique posterior position behind the spines as illustrated.

In addition to the case studies illustrated in Figs. 51 to 56, we have investigated the type of pelvis associated with spontaneous face to pubes deliveries. As a rule, the pelvis reveals one or more of the following characteristics:

1. An ample, but fairly typical anthropoid pelvis, with a subpubic angle of any size.
2. An ample android pelvis with a long fore pelvis which introduces the anthropoid tendency.
3. A definitely narrow angle in the fore pelvis at the inlet, with a posterior pelvis conforming to the gynecoid, android, or anthropoid type.

4. Converging side walls of the fore pelvis, with a narrow subpubic angle.
5. An obtuse lumbosacral angle, with a pelvic canal similar in shape to the example illustrated in Fig. 52.

The pelvis associated with a persistent occipitoposterior position which requires some form of operative delivery displays, as a rule, a combination of several of the characteristics listed above. The shape of the pelvic canal, as viewed from the lateral aspect, tends to conform to the example illustrated in Fig. 54, in which the acute angle at "A" prevents an efficient uterine drive along the fetal axis into the posterior pelvis.

#### REFERENCES

- (1) *Caldwell, W. E., and Moloy, H. C.*: AM. J. OBST. & GYNEC. 26: 479, 1933.
- (2) *Caldwell, W. E., Moloy, H. C., and D'Esopo, D. Anthony*: AM. J. OBST. & GYNEC. 28: 482, 1934.
- (3) *Caldwell, W. E., Moloy, H. C., and D'Esopo, D. Anthony*: AM. J. OBST. & GYNEC. 28: 824, 1934.
- (4) *Hodge, Hugh L.*: The Principles and Practice of Obstetrics, Philadelphia, 1864, Blanchard and Lea.
- (5) *Fabbri, Sabatier, and Pinard*: Quoted by Milne Murray and Parvin.
- (6) *Parvin, Theophilus*: The Science and Art of Obstetrics, Philadelphia, 1895, Lea, Broekers & Co.
- (7) *Murray, R. Milne*: The Transactions of the Edinburgh Obstetrical Society, Vol. XVI, 58, 1890-91.
- (8) *Hirst, Barton Cooke*: A Text-Book of Obstetrics, Philadelphia, 1918, W. B. Saunders Company.
- (9) *Bedford, Gunning S.*: The Principles and Practice of Obstetrics, New York, William Wood & Company, p. 21.
- (10) *Williams, J. Whitridge*: Obstetrics, New York, 1930, D. Appleton-Century Company.
- (11) *DeLee, J. B.*: Principles of Obstetrics, Philadelphia, 1933, W. B. Saunders Company, p. 180.

875 PARK AVENUE

---

**Farber and Hubbard: Fetal Endomyocarditis: Intrauterine Infection as the Cause of Congenital Cardiac Anomalies, Am. J. M. Sc. 186: 705, 1933.**

In the hearts of a number of infants who showed evidences of congenital heart disease at postmortem examination, the authors have found areas of fibrosis, cellular infiltration, and calcium deposition. These changes, they believe, represent the end-results of inflammatory processes which, in view of the age of the patients, must have occurred during intrauterine life.

Classifications of congenital heart disease usually list the various anomalies under two general headings: (1) Those due to primary defective or arrested development, and (2) those due to infection transmitted to the fetus from the mother at some time after the third fetal month, when the heart is believed to assume its adult form. In these cases, the septa are free from defect, the essential relationships of the chambers and great vessels are normal and the chief abnormalities consist of stenosis, or atresia of the valves. It is now generally accepted that myocardial changes are also of importance. Careful investigation of the myocardium in most cases of atresia of the orifices will reveal patchy yellowish gray areas visible to the naked eye, which microscopically show all stages of degeneration, vacuolation, fatty change, calcification with cellular infiltration, and a diffused fibrosis, which is often myxomatous in character. Four cases are reported.

J. THORNWELL WITHERSPOON.

## THE TREATMENT OF CARCINOMA OF THE CERVIX BY WERTHEIM'S OPERATION\*

VICTOR BONNEY, M.S., B.Sc., F.R.C.S., LONDON, ENG.

I ESSAYED my first Wertheim's operation in 1907 and from then up to the present time I have performed it 483 times. From the beginning the operation I have performed has been as drastic as possible including the removal of most or all of the vagina and the routine extirpation of the regional glands. Except where the patient was very old or the subject of advanced cardiac, pulmonary, renal, or other systemic disease, I have operated whenever I thought there was any chance of completing the operation. This practice has compelled me to cope with many growths at the very limit of operability and on various occasions to close the abdomen without attempting the obviously impossible, or desisting from the attempt after it was begun.

The principle I have worked on has had the disadvantage of raising both the operative mortality and the recurrence rates, but on the other hand it has enabled me to save lives that would otherwise have been lost and to present results which I believe represent the limit to which pure surgery can go in the treatment of carcinoma of the cervix.

I have not employed preoperative radiation, but a few of my earlier cases were sent to me as having been "rendered operable" by radium. The operations were exceedingly difficult and none of the patients survived five years. I have employed postoperative radiation only in those cases where it was found impossible to remove carcinomatous glands from the iliac vessels. Not one of these patients survived five years. The successes I am able to record are therefore the fruit of surgery and surgery only.

I will first give you my results on the basis of five years' freedom from recurrence so that they may be compared with the statistics of radiology, and afterward on the basis of ten years' freedom from recurrence, because 10 per cent of all recurrences appear between the fifth and tenth year. Five years' freedom from recurrence is only a 90 per cent cure, but ten years' freedom is a 100 per cent.

I have classified my cases according to whether the regional glands removed at the operation were or were not carcinomatous. Such a classification gives a good indication of the average advancement of the primary growth in the two groups respectively; but though in

\*Read, by invitation, at the Sixtieth Annual Meeting of the American Gynecological Society, Hot Springs, Va., May 27 to 29, 1935.



eases in which the regional glands are involved the primary growth in the cervix is on the average of older standing and more extensive than in cases in which the regional glands are not involved, there is no hard and fast rule and extensive glandular involvement may co-exist with a very small primary growth in the cervix, whilst conversely the cervical growth may be most extensive without any involvement of the regional glands. I have not adopted the classification that obtains in radiology, in the first place because my series was begun before radiology appeared in the field, and in the second because no useful comparison can be drawn between what one man sees and another man thinks he feels.

#### RESULTS ON THE FIVE-YEAR BASIS, 1907-1929

Died of operation	55
Lost sight of within five years	12
Died other diseases within five years	12
Recurrence within five years	155
Well after five years	150
	<hr/>
	384

The operative death rate of this series is 14 per cent. It was 20 per cent in my first hundred operations but has progressively fallen owing to increased experience and various precautions. For the last 200 operations I have performed it is 9.5 per cent.

If the patients lost sight of and dying of other disease within five years of the operation are reckoned as having died of recurrence the five-year cure rate is 39 per cent, or if (as I think more properly), they be dismissed from the calculation, between 41 and 42 per cent.

#### RESULTS ON THE FIVE-YEAR BASIS CONTINUED, 1907-1929

The effect of glandular involvement:

	GLANDS NOT INVOLVED	GLANDS INVOLVED
Died of operation	22	33
L. S. O. within five years	6	6
Died other disease within five years	10	2
Recurrence within five years	71	84
Well after five years	114	36
	<hr/>	<hr/>
	223	161

It will be noted that the regional glands were carcinomatous in 42 per cent of the cases. This figure roughly accords not only with the gland involvement rate of all my cases but also with that of the cases operated on by my colleague, Comyns Berkeley. It goes up and down a little according to the incidence of chance, but it can with certainty

be said that of the patients presenting themselves with carcinoma of the cervix at least 40 out of every 100 already have carcinoma in the regional glands. The difference in the prognosis of the two groups is very striking. The cases whose regional glands were growth-free ran on the average an operative death risk of 9.8 per cent, in return for which they gained, depending on which of the two reckonings referred to is employed, a 51 or 55 per cent chance of five-year survival; whereas on the average cases whose regional glands were carcinomatous ran a death risk of 20 per cent to gain a 22 or 23 per cent chance of five-year survival. On the other hand the contention of certain authorities that the routine removal of regional glands is unwarranted because cases in which they are carcinomatous almost always die of rapid recurrence is disproved, for my figures show that about 23 per cent of these gland-involved cases may be expected to survive five years.

Up to the end of 1924 I had performed Wertheim's operation 283 times with the following results:

RESULTS ON THE TEN-YEAR BASIS, 1907-1924

Died of the operation	47
Lost sight of within ten years	23
Died of other disease within ten years	12
Recurrence within ten years	119
Well after ten years	82
	<hr/>
	283

The operative death rate of this series is 16 per cent, a higher figure than that of the series previously dealt with because it contains a larger proportion of my early cases. The proportion of cases lost sight of is increased owing to the difficulty of keeping in touch with patients over so long a period. Similarly there is an increased proportion of deaths due to causes other than recurrence. The labor of keeping in touch with my patients has been mine, for it is only of quite recent years that follow-up departments have been instituted in Great Britain, and even now they are imperfect. The reason is the expense which places another burden on institutions already financially strained. If these patients who were lost sight of and dying of other disease are reckoned as having died of carcinoma the ten-year cure rate is 20 per cent, but if they be dismissed from the calculation, as in my opinion they certainly should be, it is 33 per cent. Ten-year cures are to be regarded as absolute cures. It is not, of course, impossible for recurrence to take place after that lapse of time, but I have not met with it.

## THE EFFECTS OF GLANDULAR INVOLVEMENT

## RESULTS ON THE TEN-YEAR BASIS CONTINUED, 1907-1924

	GLANDS NOT INVOLVED	GLANDS INVOLVED
Died of operation	19	28
L. S. O. within ten years	17	6
Died other disease within ten years	10	2
Recurrence within ten years	53	66
Well after ten years	59	23
	<hr/> 158	<hr/> 125

As in the five-year series there is a marked difference in the results obtained from the two groups. The operative mortality of the gland-free group is 12 per cent as against 22 per cent for the gland-involved group, while, according to the method of reckoning, the ten-year cure rate is 37 or 45 per cent as against 18 or 20 per cent. The higher gland involvement rate (44 per cent) must be fortuitous, for my method of selection has never varied, nor have I observed that patients in more recent years present themselves earlier in spite of modern propaganda.

## ACTUAL OPERATIVE ACHIEVEMENT

In order to assess the actual achievement of any series of operations for carcinoma it is necessary to know the surgeon's operability rate, i.e., the percentage of patients selected for operation out of every 100 seen. For some years after Comyns Berkeley and I had begun to perform the operation, we were able to estimate our operability rate with accuracy at 63 per cent, for we were the only surgeons in our hospitals performing the operation at that time, and we had complete command over the clinical material presented to us. In later years, however, for several reasons we lost that command and it became impossible to disentangle the cases in which we determined the treatment from those in which the treatment had been determined by others. In all our subsequent communications we continued to reckon our operability rate as being 63 per cent, feeling justified in doing so because our operative practice never varied.

There is one group of my cases on which I can speak with complete certainty in this matter, namely, the patients whom I have seen in my consulting room and over whose treatment I have therefore had entire determination. Between the years 1907 and 1930 I operated on 80 per cent of these. In the reckoning of my actual operative achievement which I am now going to give you I shall assume as heretofore my operability rate to be 63 per cent.

On the basis of five years' freedom from recurrence my actual operative achievement is 24.6 per cent if the cases lost sight of and died of

other disease within five years are reckoned as having died of recurrence, or 25.6 per cent if they are excluded from the calculation; while on the basis of the ten years of freedom from recurrence the figures are 18 per cent, or just on 20 per cent. The value of the operation may therefore be briefly expressed by saying that on the five-year basis it cures 2 out of every 5 patients operated on, and 1 out of every 4 patients seen; whilst on the ten-year basis it cures one out of every 3 patients operated on and 1 out of every 5 patients seen.

It is apt to be forgotten that the number of cures effected by the operation is not the same thing as the number of cures to the credit of the surgeon who practices it, for besides those patients he operates on there remains a residuum which he treats by radiation. If he operates on 63 out of every 100 patients presented to him there are 37 of these.

Except for a small proportion where the operation was forbidden not because it was mechanically impossible but on account of the woman's general physical state, all these patients are the subject of advanced disease and come under Class III and IV of the Radiological Classification. Five of these 37 patients, i.e., 5 per cent of the 100 originally seen, may be dismissed from consideration as beyond the reach of any measures. Out of the 32 remaining a certain proportion of five-year cures can be obtained by radiation; judging from Radiological statistics about 5, and this number has to be added to the number of five-year cures by operation. A surgeon, therefore, who deals with his cases of carcinoma of the cervix as I have dealt with mine may expect to obtain 29 to 30 five-year cures out of every 100 unselected cases that he sees.

The operation as I do it is performed as follows:

Under full ether and spinal anesthesia the patient is placed in the lithotomy position, and a catheter having been passed, the vagina is tightly packed from the vault downward with gauze soaked in "Violet-Green."\* The patient is then fixed in the Trendelenburg position and the abdomen is opened in the middle line.

Ligatures are now placed on both ovario pelvic ligaments and on both round ligaments, and a clamp having been placed just outside the uterine cornu on each side, the upper parts of the broad ligaments are divided just inside the ligatures (Figs. 1, 2, and 3).†

The freed appendages are now ligatured as they come off from the uterus, and the ends of the ligatures are left long. A forceps is placed on the ends, thus making a convenient tractor (Fig. 4).

The peritoneum across the front of the uterus is now divided and an anterior flap is reflected until the bladder is reached. The bladder is now separated from the vagina partly by thumb pressure and partly by scissors (Fig. 5).

\*One per cent of equal quantities of crystal violet and brilliant green dissolved in equal parts of 95% alcohol and water. A 1 per cent solution of flavine in water can be used if "violet-green" is not available.

†The illustrations have been redrawn by Mr. Bonney from the *Textbook of Gynecologic Surgery*, by Sir Comyns Berkeley and Victor Bonney, Cassel & Co., London, 1935.

The separation at this stage should not be continued further than an inch downward, for it is better to effect the complete separation step by step as the operation proceeds.

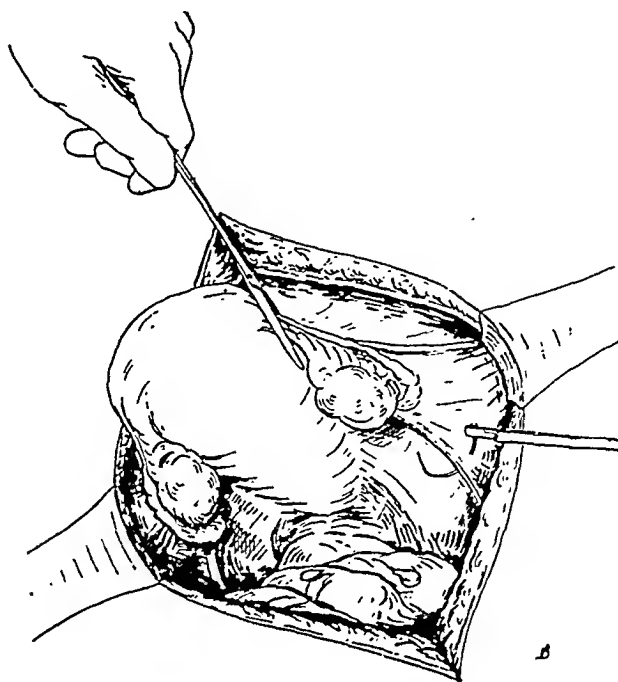


FIG. 1.

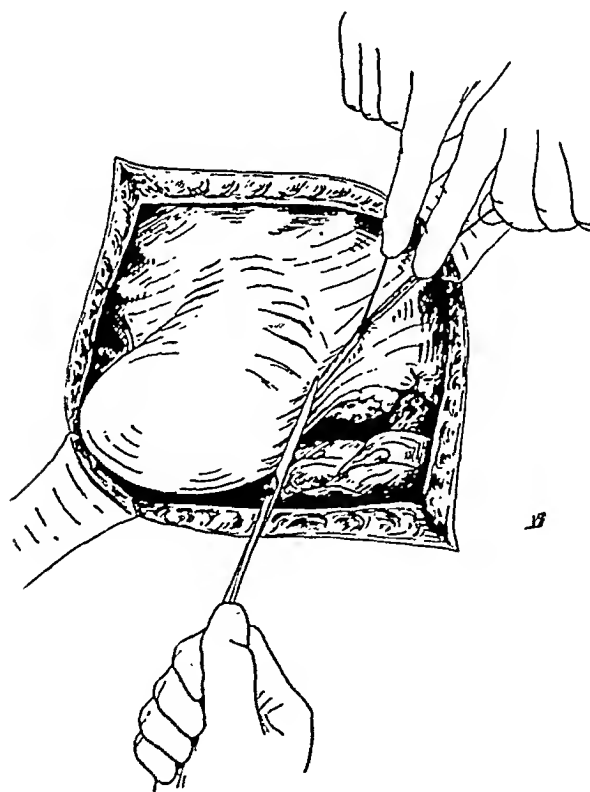


FIG. 2.

The peritoneal flap should be sutured to the lower angle of the abdominal wound to keep it out of the way.

The next step is to open up the broad ligament and define the external iliac vessels. To do this forceps should be attached to the stumps of the ovario-pelvic and round ligaments and the loose areolar tissue of the broad ligament teased aside until the vessels are clearly seen.

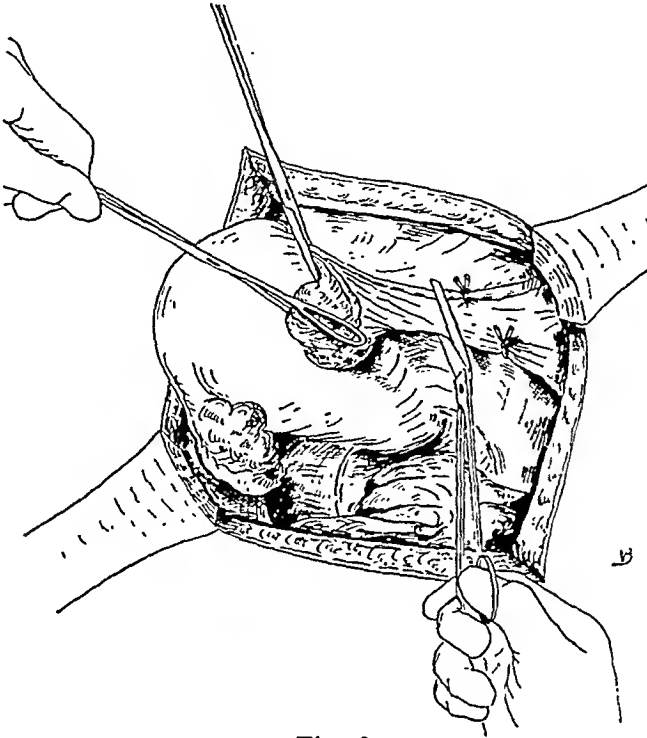


Fig. 3.

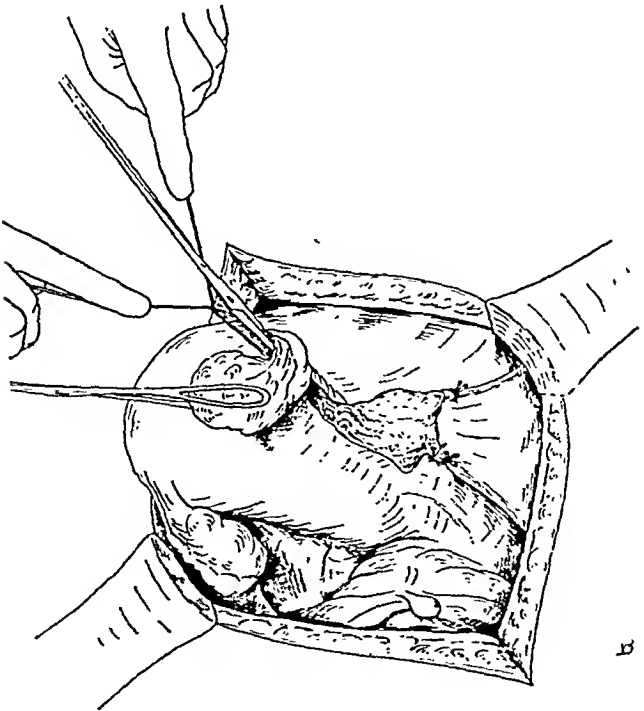


Fig. 4.

The ureter should now be felt for with the thumb and index finger on either side of the posterior layer of the broad ligament to which layer the ureter clings. It can generally be seen as well as felt (Fig. 6).

The uterine artery is now sought. The internal iliac artery and its continuation forward as the hypogastric must first be defined. The uterine artery comes off the hypogastric artery, usually at right angles, and, in easy cases with a little teasing aside of the areolar tissue, is readily seen (Fig. 7). In more difficult cases the index finger should be thrust down into the broad ligament between the ureter previously

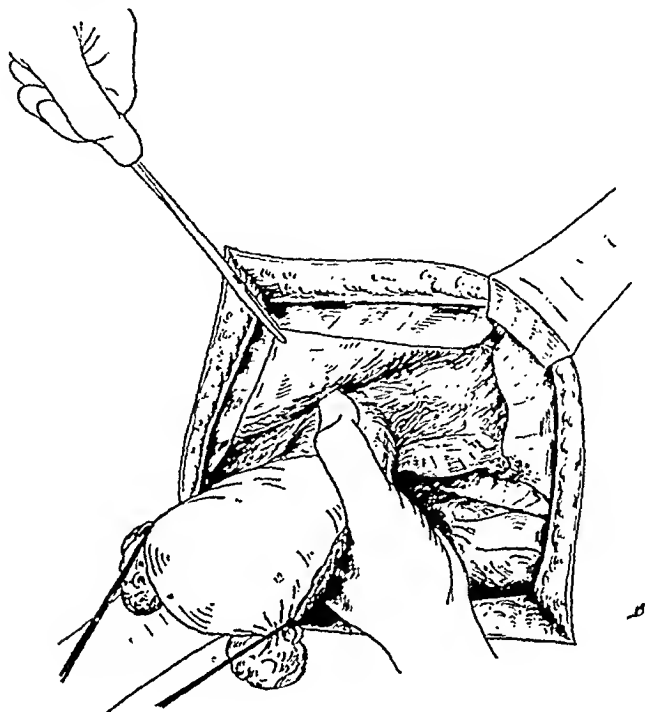


Fig. 5.

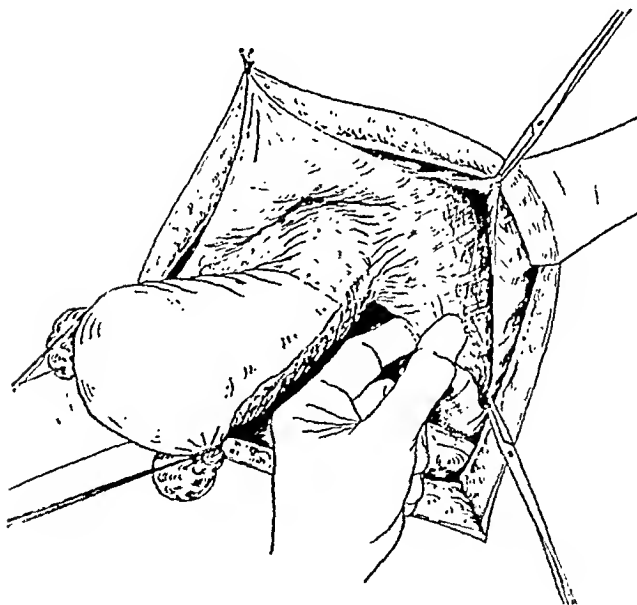


Fig. 6.

defined and the internal iliac artery also previously defined, and the fingertip exploring forward is made to underburrow and hook up the artery which with a little experience can easily be felt.

The artery is now divided between two forceps, and the uterine end being rucked back, the ureter will be perceived running under it (Fig. 8). It should be followed up until it disappears into the ureteric canal.

The tip of the left index finger is now pushed along the canal and the roof of the canal cautiously divided (Fig. 9). The tissue inside the ureter which holds it against the vagina is now divided down to the ureterovesical junction, and the ureter is rolled outward and finally completely raised from its bed, though the length of this raising should be kept as short as possible (Fig. 10).

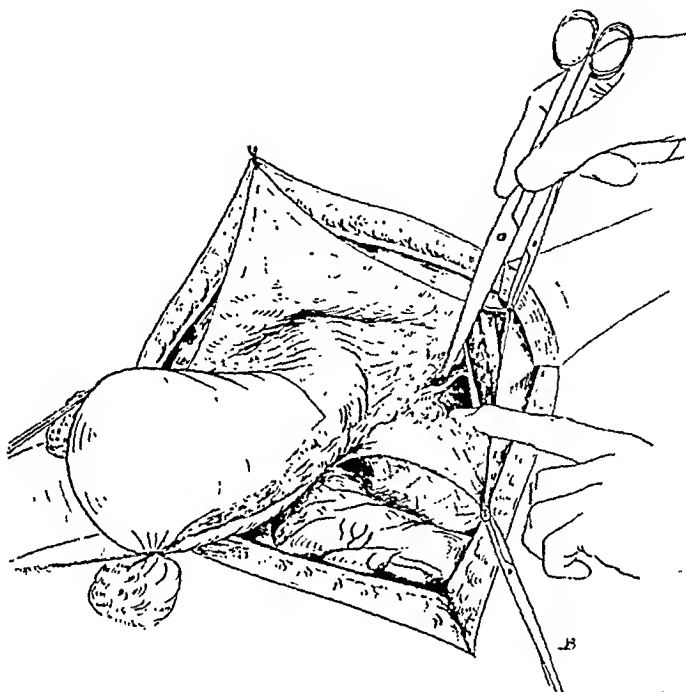


Fig. 7.

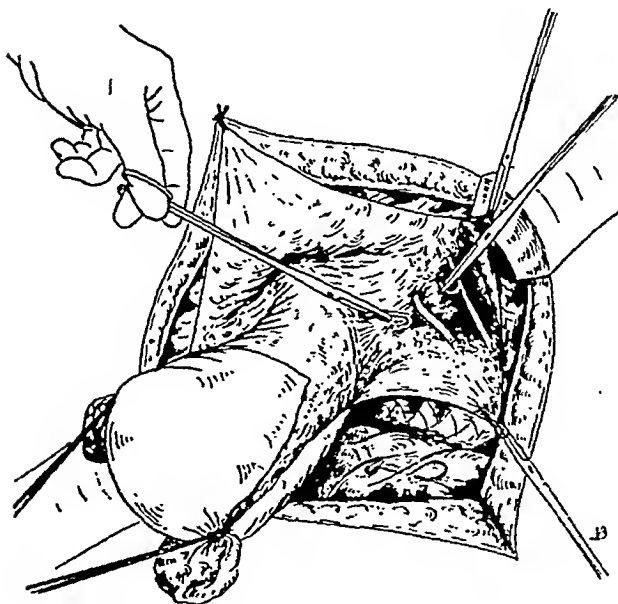


Fig. 8.

The same procedures are then carried out on the opposite side.

The uterus is now carried forward and the loose peritoncum on the front wall of Douglas' pouch is picked up and divided (Fig. 11).

The index and middle fingers of the left hand are now insinuated between the vagina and rectum, keeping the pulps against the packed column of the vagina until the two canals are separated almost or quite down to the pelvic floor (Fig. 12).



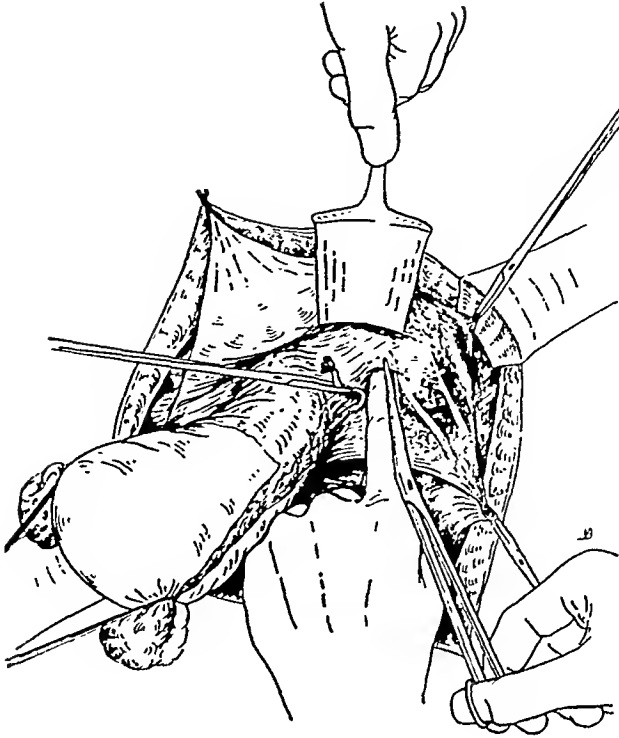


Fig. 9.

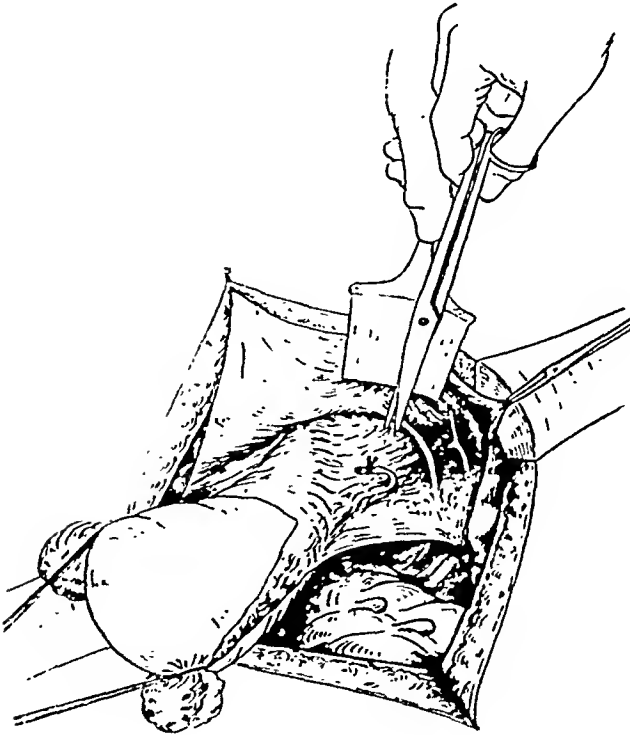


Fig. 10.

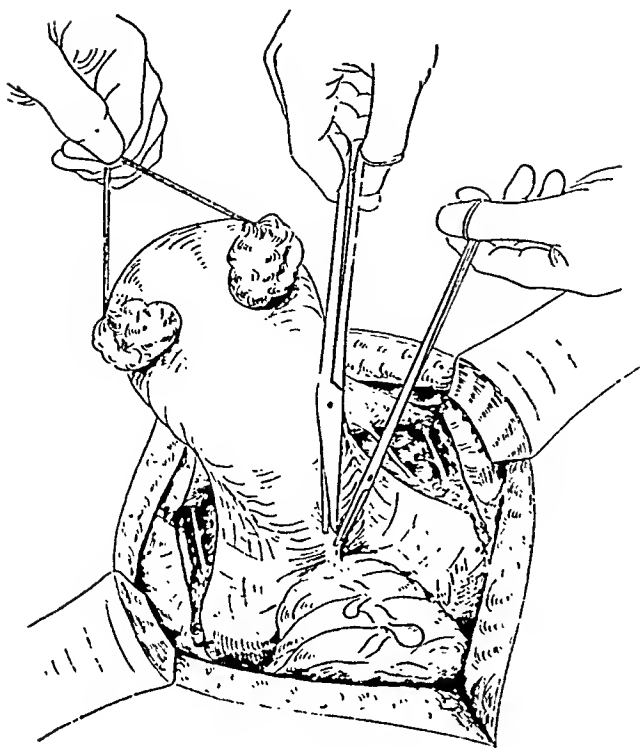


Fig. 11.

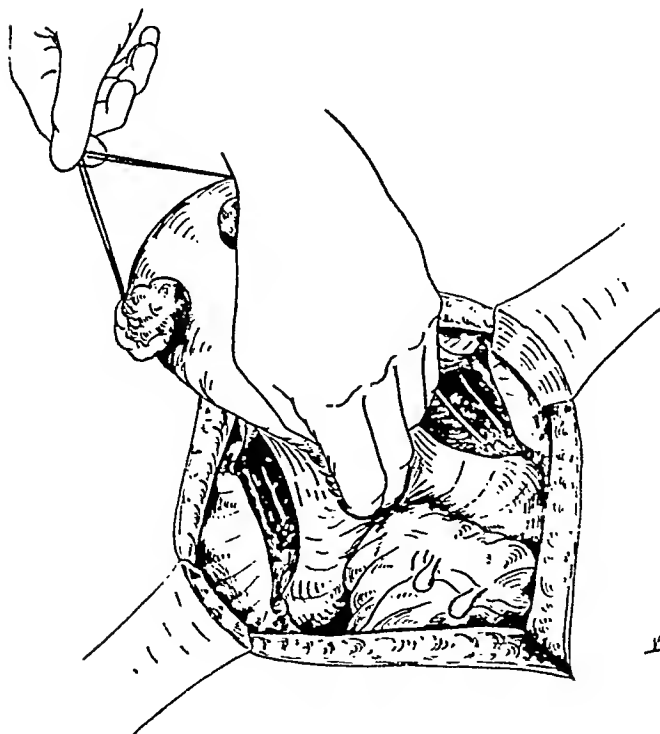


Fig. 12.

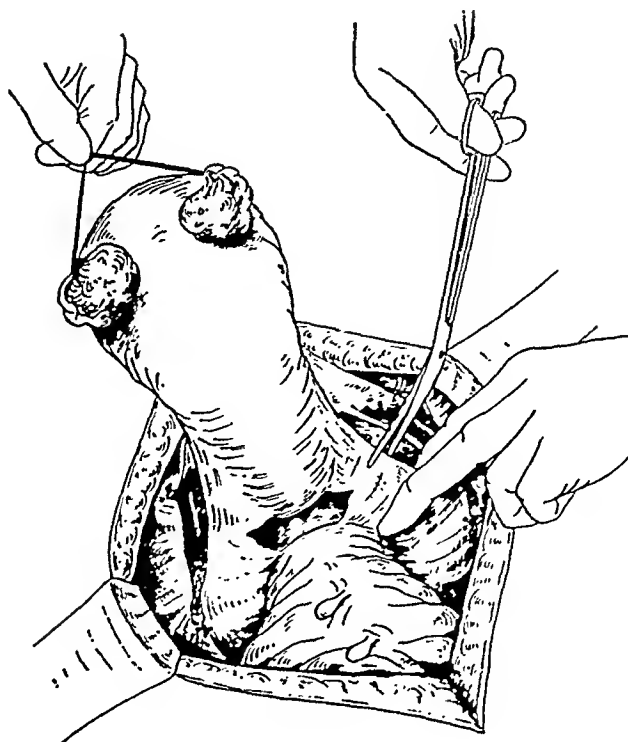


Fig. 13.

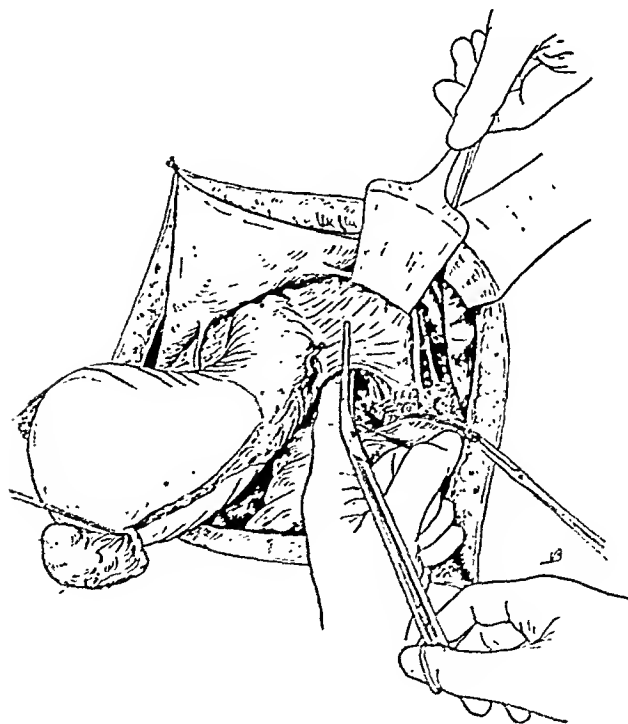


Fig. 14.

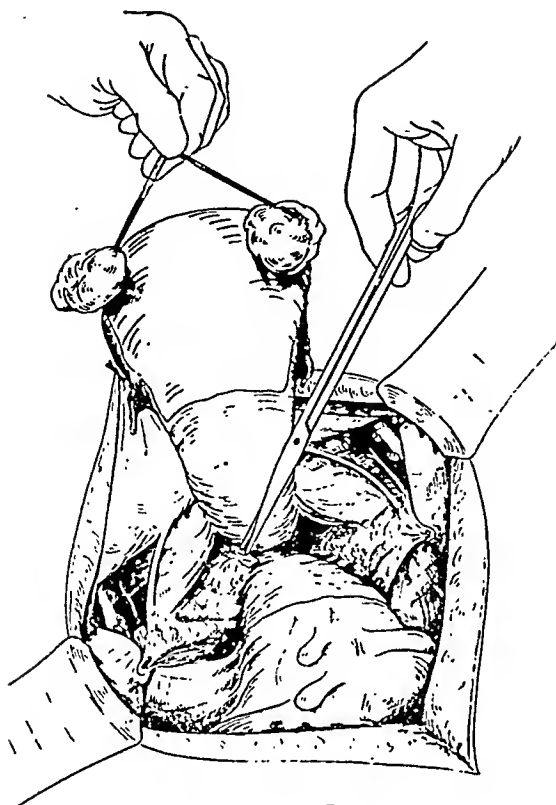


Fig. 15.

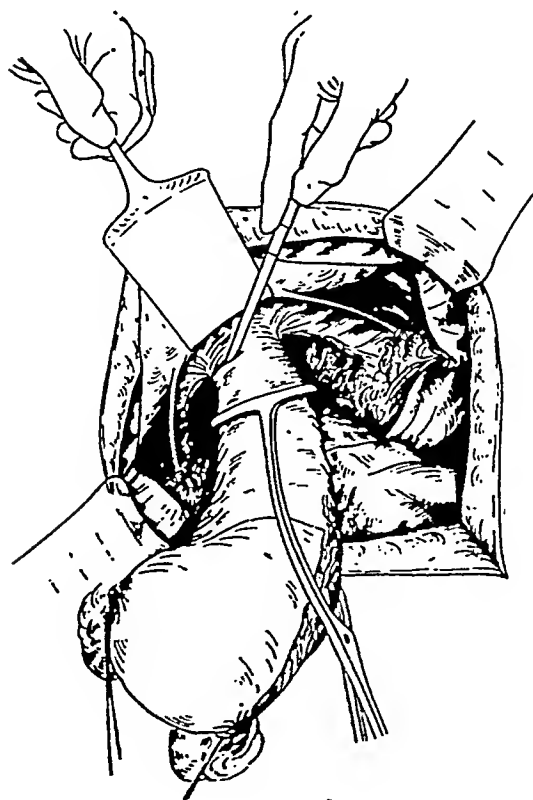


Fig. 16.

The remainders of the posterior peritoneal layers of the broad ligaments are now divided to meet the aperture in Douglas' pouch, care being taken not to divide the ureters which must be defined before using the seissors (Fig. 13).

The cardinal ligaments of the vagina are now accessible, to which achievement all the preceding steps of the operation have been leading up. They can be felt as two broad fan-shaped sheets extending from the sides of the vagina outward. The index finger of the left hand should be passed behind one of them and the ureter, which lies on it, having been thoroughly displaced outward and kept there by a retractor, the ligament is cautiously divided over part of its depth (Fig. 14).

A similar procedure is then carried out on the opposite side.

The uterus is then carried forward again and a further separation of the rectum and the tissues lateral to the rectum is carried out (Fig. 15) after which the cardinal ligaments are again turned to and still further divided. It is better to effect this division gradually, turning first to one side and then to the other. The severance should be carried out until the whole depth of the ligaments, or nearly the whole

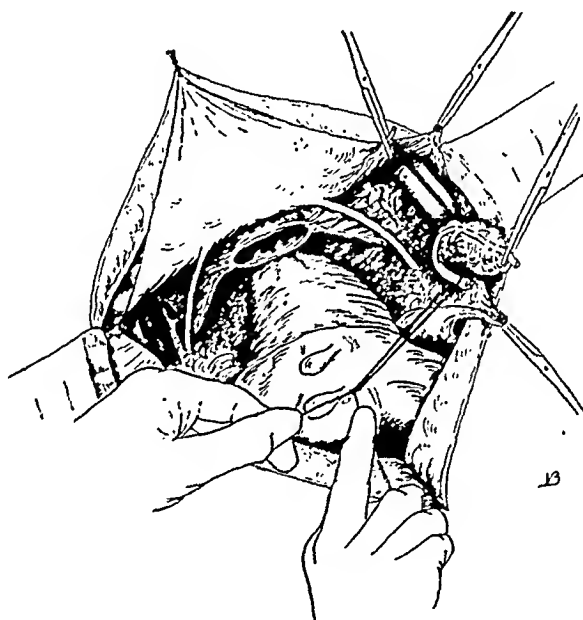


Fig. 17.

depth, down to the pelvic floor is divided. During the process the surgeon should alternate cutting the cardinal ligaments with further separation of the bladder, not only in the middle line but outward somewhat beyond the ureterovesical junctions.

The uterus and vagina are now only held by the attachment of the lower end of the latter to the pelvic diaphragm. The gauze in the vagina having been withdrawn, a Berkeley-Bonney clamp is applied well beneath the growth and the vagina divided as low down as the separation makes possible (Fig. 16). As a rule practically all the vagina is removed so that when the patient subsequently presents herself for inspection, the formation is similar to what obtains in a case of "imperforate hymen." It will be noted that no clamps are placed on the cardinal ligaments before division. They are unnecessary and hamper the operator. If a vessel bleeds during the division it should be picked up with forceps.

As soon as the removal is effected the pelvis should be wiped clear of blood and obviously bleeding vessels picked up and tied. It is a good thing as a routine to place a strong mattress ligature on the tissues immediately outside the lateral vaginal angle on either side, as there are nearly always bleeding vessels in these situations.

The regional glands are now to be removed. Those along the external iliac vein

should be separated inward and then raised together with the hypogastric artery. The artery is then divided at the lateral angle of the bladder and rucked back with the glands until the mass pivots on the anterior trunk of the internal iliac artery. This is then ligatured and divided (Fig. 17).

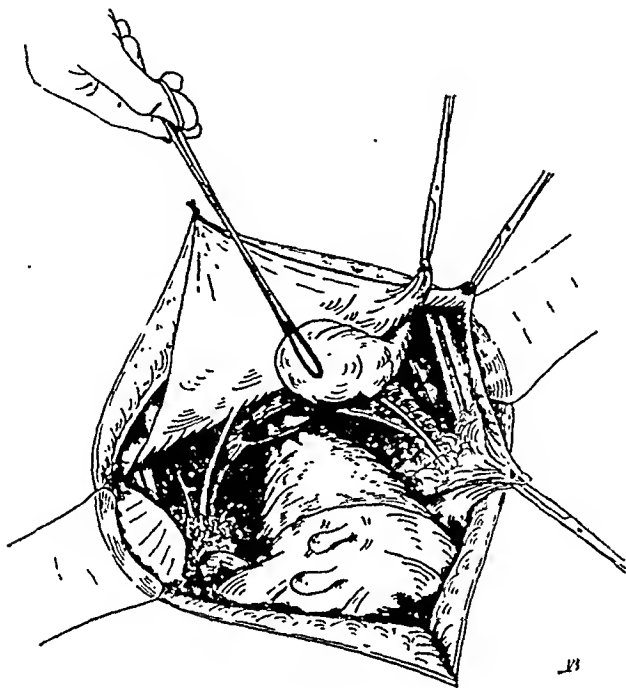


Fig. 18.

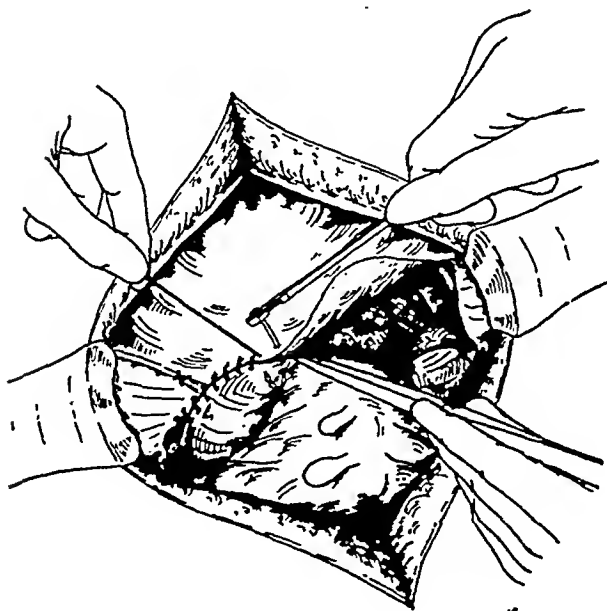


Fig. 19.

In early cases it is not necessary to do this, and the glands should be dissected off by themselves.

There now remain the glands in the obturator fossae. It is important to remove these as they are the first group to become invaded. They lie in a mass of fat which can both be seen and be felt inside the line of the hypogastric artery and below the external iliac vein. The obturator nerve passes through the mass of fat. The best way to separate this mass is by the fingers aided by "ring forceps."

With practice it can be extracted very cleanly and without bleeding. The obturator nerve should be separated out of it unless it is involved in growth. The mass of fat extends by a process downward to the brim of the pelvis under Poupert's ligament and when extracted the bare bone of the pelvis should be felt (Fig. 18).

The vagina, or rather what remains of the vagina, is left open and through it a strip of thin gauze previously soaked in flavine 1 in 1,000 is passed until it protrudes from the vulva. The rest of the length of gauze (about 2 feet) is lightly packed into the pelvis, after which the peritoneum is united across the pelvis by a continuous suture (Fig. 19). The gauze is removed via the vulva in from forty-eight to seventy-two hours.

Convalescence is conducted on the usual lines, but absolute retention of urine for from one to two weeks and sometimes longer always occurs and compels the regular use of a soft rubber catheter.

15 DEVONSHIRE PLACE

---

## TUBERCULOSIS OF THE CERVIX UTERI\*

VIRGIL S. COUNSELLER, M.D., AND DONALD C. COLLINS, M.D.,  
ROCHESTER, MINN.

**T**UBERCULOSIS of the cervix uteri is very rare. We have partially reviewed the literature on this condition, and are reporting a complete study of a case, which was seen at the Mayo Clinic, in the hope that it may assist in the prompt recognition and early institution of adequate treatment.

Morgagni in 1744 was the first to describe tuberculous salpingitis and tuberculous endometritis; in his case, the patient was a girl, aged twenty years. He concluded that tuberculous pelvic disease may be the source of a generalized tuberculous peritonitis. Lisfranc is said to have presented the first case of tuberculosis of the cervix. In 1834 Boivin and Dugés wrote an excellent atlas of diseases of the uterus and its adnexa. In this work they clearly described for the first time a true instance of tuberculosis of the cervix uteri. Nine years later, Louis reported a clinical example of this condition. Kiwisch in 1847 described this disease with remarkable accuracy and clearly demonstrated his clinical knowledge of this condition. Geil completed his classic work on "Tuberculosis of the Female Genital Organs" in 1851. Little has been added to his description in the following eighty years.

Rudolph Virchow in 1853 carefully described instances of tuberculosis of the cervix. Friedländer shortly thereafter described another similar instance of primary tuberculosis, and his contention was verified by necropsy after the patient had died of an apoplectic seizure. At this point Rokitansky "muddied the waters" by declaring that tuberculosis of the cervix never occurred. So great was his authority that further investigation was stifled. Ten years elapsed before Lancereaux and Lackerbauer demonstrated beyond argument that tuberculosis of the cervix did exist and that it was usually secondary to pulmonary tuberculosis. In the following year, 1872, Lebert reaffirmed Rokitansky's opinion. His contentions were based upon only thirty-three cases of tuberculosis of the uterus and its adnexa,

---

\*From the Mayo Clinic and the Mayo Foundation.  
Submitted for publication January 18, 1935.

which he had observed personally. As later investigations have demonstrated, his series of cases was entirely too small to warrant such sweeping conclusions.

The next important contribution was made by Cohnheim in a small book, which was published in 1879. He said that tuberculosis of the cervix could easily result from coitus with a tuberculous partner. This immediately popularized the entire subject and once again focused considerable attention upon it. Two years later, Lukasiewicz and Mayor reported examples of secondary tuberculous involvement of the cervix, in which there was an accompanying tuberculous endometritis. In 1883 Verneuil independently made observations, which were similar to those of Cohnheim. In this same year, Babés isolated the tubercle bacillus from the vaginal secretions of a patient, who had tuberculosis of the cervix, and definitely settled once and for all the etiology of this disease. In the following six years cases were reported by Winters, Derville, Cornil, Zweighaum, Thiereclin, and Schmorl and Bireh-Hirschfeld. In 1892, J. Whitridge Williams presented an exhaustive survey of this subject; this was one of the first reports to come from America. Additional data were added by Emanuel, Meyer, Sippel, Kaufmann, Weigert, Vassmer, and Ajello.

Beyca in 1901 completely reviewed the literature up to that date and tabulated his findings. He was able to collect 68 cases of proved tuberculosis of the cervix. Thirty of these were proved at necropsy, and were associated with advanced tuberculosis elsewhere in the genital tract. Two instances were found of primary involvement of the cervix. Twenty-two cases were observed clinically; 9 of these were believed to be cases of primary infection. Fifteen of the entire 68 cases were studied both clinically and at necropsy; all of these cases were found to have foci of active tuberculosis elsewhere in the body. Thirty-six of 57 patients were found to be between twenty and forty years of age, which is the period when the female genital tract is at the height of its functional activity. In a group of 56 cases, the correct diagnosis of tuberculosis was made in 28 cases, while the diagnosis of malignancy of the cervix was made in 17 cases.

In the next two years, additional cases and important data were presented by Horrocks, Croft, Levers, Brook, and Kynock. John B. Murphy in 1903 and 1904 exhaustively reviewed this entire subject and brought all the data up to date. His contributions to this field were thorough and little has been added to our knowledge since his publications. Four years later, Vineberg was able to find only 22 cases of primary tuberculosis of the cervix recorded in the literature. He added a secondary case. Neu urged the employment of radical surgical procedures to bring about the highest percentage of permanent cures. Horizontow said that in 14 per cent of his specimens of pelvic tuberculosis the cervix uteri was involved. In 1916, Cullen reported a very early example of this disease in the case of a young negress, who complained of the spontaneous development of a rectovaginal fistula that had been present two years. Moore presented an excellent review of the literature up to 1919 and added an additional case of the secondary type.

Greenberg, in a review of the literature, in 1920 reported that in a series of 897 cases of pelvic tuberculosis there were 37 cases (4.2 per cent) that revealed tuberculosis of the cervix uteri. Norris, Wharton, Spalding, Neuwirth, Culbertson, Daniel, Schmidt, Pavlovsky, Bengolea and Pavlovsky, Gupta, Douglas and Ridlon, White, Bishop, Harris, Dworzak, and Bonnet and Builliard made notable contributions to this field in the next eleven years. Davis studied 1,200 cervixes, which had been removed surgically; 777 of these disclosed evidence of inflammation, but the inflammation was tuberculous in only one specimen. On the other hand, 25 (5.7 per cent) additional specimens of this same group were carcinomatous. In the last two years, noteworthy articles upon this subject have been presented by Sasaki, Davis, and Watson.



In 981 reported cases of genital tuberculosis among women, there were 39 (0.4 per cent) instances of tuberculosis of the cervix. Of these 39 examples, 3 (7.7 per cent) were undoubted primary tuberculous infections. About 40 per cent of the recorded cases of tuberculosis of the cervix were associated with active pulmonary tuberculosis. Williams expressed the opinion that one of every 600 women who had tuberculosis of the lungs, later developed tuberculosis of the cervix. In the pathologic examination of 22,335 operative specimens reported in the literature, there were only 4 (0.027 per cent) proved examples of this disease. At the clinic, we were able to find only 1 case of this condition which was definitely proved; this case we are reporting together with 3 cases which are very doubtful, and which apparently are not tuberculous.

Babés in 1883 definitely demonstrated that the tubercle bacillus was the etiologic agent in this condition. He found and demonstrated Koch's bacillus in the vaginal secretions obtained from a patient who had this disease. Beyea found that in 63 per cent of the cases reported in the literature, the patients were between twenty and forty years of age. In the 108 cases which we have been able to study in the literature (Table I), this percentage was further increased to 73.5. In this series, 10 cases (9.25 per cent) were undoubtedly of primary origin, while 5 additional cases (4.63 per cent) were of doubtful primary character. Beyea found 2 (2.94 per cent) cases of proved primary type and nine (13.4 per cent) of doubtful primary origin in a group of 68 cases recorded in the literature up to 1901. In 1919 Moore estimated that the literature contained reports of 170 cases of tuberculosis of the cervix, of which 20 (11.7 per cent) were of primary type. Harris, however, believed that there were actually fewer cases which were really primary. Bishop said that less than 25 proved cases of primary tuberculosis of the cervix had been reported.

Tuberculosis of the cervix is, in at least 85 per cent of cases, secondary to tuberculosis elsewhere in the body, as in the fallopian tubes, urinary tract, gastrointestinal tract or in the lungs. In the 108 cases which we have studied, 78 per cent had accompanying tuberculosis elsewhere in the generative tract, while 82 per cent of the secondary cases had demonstrable pulmonary tuberculosis, either in a quiescent or active state. Many of these patients gave a family history that was positive for phthisis. Pregnancy and marriage are two prominent contributing factors in the onset of the disease. Bishop said that Jung, Bennecke, and Hashimoto had demonstrated in experimental animals that it is possible to infect the cervix uteri first, and subsequently the fallopian tubes with tuberculosis, or vice versa, and yet have the endometrium remain free of the infection. This fact has been frequently reported in the literature. The order of frequency of tuberculous infection in the female generative tract, from the most common to the least common, is as follows: fallopian tubes, endometrium of the uterus, cervix uteri, vagina and vulva. Thus, secondary tuberculous infection of the cervix usually indicates that it was derived from a descending infection originating from foci higher in the pelvis.

The criteria for primary tuberculosis of the cervix demand that it be the only tuberculous infection in the body. Hence, as Murphy has demonstrated, it must usually be an ascending infection, which has been derived from the vagina or vulva, or more commonly from a tuberculous

TABLE I. RÉSUMÉ OF CASES REPORTED IN THE LITERATURE

YEAR	AUTHOR	NUMBER OF CASES, GENITAL TUBERCU- LOSIS	SOURCE OF MATERIAL	TUBERCULOSIS OF CERVIX	
				NUMBER OF CASES	PER CENT
1834	Boivin and Dugés	?	Necropsy	2	?
1842	Lisfranc	?	Necropsy	1	?
1853	Virehow	?	Necropsy	2 (1 Primary)	?
	Weigert	?	Necropsy	2 (1 Primary)	?
	Friedländer	?	Necropsy	1 (1 Primary)	?
1872	Lebert	33	Clinical	0	0.0
1881	Lukasiewicz	?	Clinical	1	?
1881	Mayor	?	Clinical	1	?
1885	Spaeth	119	Clinical	6 (1 Primary)	5.0
1887	Derville	?	Clinical	1	?
1887	Winters	?	Clinical	1	?
1888	Cornil	?	Clinical	1	?
1888	Zweigbaum	?	Necropsy	1 (Primary)	?
1889	Thierceclin	?	Clinical	1	?
1891	Schmorl	?	Necropsy	2	?
1892	Williams	?	Clinical	2	?
1894	Emanuel	?	Clinical	1	?
1894	Meyer	?	Clinical	1	?
1897	Kauffman	?	Necropsy	1 (Primary)	?
1899	Vassmer	6	Clinical	2	33.0
1900	Ajello	?	Clinical	1	?
1901	Beyea	?	Clinical	1	?
1902	Horrocks	?	Clinical	1	?
1902	Levers	?	Clinical	1	?
1902	Croft	?	Clinical	1	6.4
1903	Berkeley	62 (7.7 %)	Necropsy (798)	4	
1903	Brook	?	Clinical	1 (Primary)	?
1904	Murphy	?	Literature, not above	9 (2 Primary)	?
1908	Vineberg	?	Clinical	1	?
1911	Kroemer	267	Clinical	11	4.1
1911	Schlimpert	73	Clinical	3	4.1
1911	Neu	82	Clinical	3	3.7
1911	Horizontow	?	Clinical	?	14.0
1912	Labhardt	73	Clinical	0	0.0
1916	Cullen	?	Clinical	1	?
1919	Moore	?	Clinical	1	?
1920	Greenberg	200	Clinical	9 (2 Primary)	4.5
1921	Norris	66	Clinical	1	1.5
1922	Spalding	?	Operative speci- mens (6,005)	1	0.016
1923	Neuwirth	?	Clinical	1	?
1924	Culbertson	?	Clinical	1 (? Primary)	?
1926	Pavlovsky	?	Clinical	1	?
1928	Gupta	?	Clinical	5 (?3 Primary)	?
1929	Douglas and Rid- lon	?	Clinical	2	?
1929	White	?	Clinical	1	?
1930	Bishop	?	Clinical	1	?
1930	Harris	?	Clinical	1 (? Primary)	?
1931	Bonnet and Builliard	?	Clinical	5	?
1932	Davis	?	Operative speci- mens (1,200 cervices)	1	0.083

TABLE I—CONT'D

YEAR	AUTHOR	NUMBER OF CASES, GENITAL, TUBERCU- LOSIS	SOURCE OF MATERIAL	TUBERCULOSIS OF CERVIX	
				NUMBER OF CASES	PER CENT
1934	Watson (Norris)	?	Clinical	1	?
		?	Operative speci- mens (15,130)	4	0.0066
	(Dannreuther) (H. Vineberg)	?	Clinical	3	?
		?	Clinical	1	?
1934	Counsellor and Col- lins	?		1*	0.0
				109 (11 true primary and 5 questionable primary)	

\*This does not include three doubtful cases which were not proved.

partner at coitus. He said that Klebs and Seanzoni absolutely denied the possibility of the occurrence of such an infection. It is a well-known fact that wives of tuberculous husbands seldom develop a primary tuberculosis of the cervix, while there are cases upon record in which this factor was the cause of a tuberculous salpingitis or tuberculous endometritis with a normal cervix. This fact was demonstrated by Cohnheim in 1879, and by Verneuil four years later.

The importance of tuberculosis of the cervix rests primarily in those cases in which little or no evidence of tuberculosis is evident elsewhere in the body. The physician first discovers the condition when he examines the cervix. The ease with which this disease may simulate carcinoma of the cervix is well known and here rests the importance of its differentiation. With an ulcerated lesion of the cervix, which grossly resembles carcinoma, the examiner would be correct 98 times out of 100 if he diagnosed the lesion as carcinoma. However, the prognosis, treatment, morbidity, and the effect upon the patient are so vastly different in the two conditions that they should be distinguished (Table II).

The four chief types of tuberculosis of the cervix uteri, named in the order of their frequency, are: ulcerative, papillary, miliary, and bacillary catarrhal. Thus, the gross picture of the cervical lesion may vary. It is usually ulcerated; the edges are either well defined or undermined, and are surrounded by either normal tissue or by tubercles. The neighboring portions of the vagina may be involved and tubercles may form. Bishop said that the earliest lesion is a polypoid process and that this is soon followed by ulceration, which may develop into a huge ulcer with ragged undermined edges. On the other hand, the tuberculous infection may be rather deep in the substance of the cervix and reveal little or no ulceration or papillomatous formation on the surface. A rare fibrosing type is occasionally seen. Secondary infection commonly is superimposed on these lesions and more or less cervical bleeding or even hemorrhages are frequently encountered.

Microscopically, typical formation of tubercles is not commonly seen. Often, atypical collections of epithelioid and lymphocytic cells, without giant cells, are the only criteria upon which the microscopic diagnosis can be made. Staining the tissue or smears from the tissue with acid-fast stains often will fail to reveal typical tubercle bacilli. Here, inoculation of guinea pigs is of great value in establishing the correct diagnosis.

TABLE II. DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS AND CARCINOMA OF THE CERVIX

CERVIX	TUBERCULOSIS	CARCINOMA
Color	Papillary type: rose red, deeper red than surroundings Ulcerated type: crater yellowish or red	Grayish
Appearance	Papillomatous or ulcerated. May be entirely interstitial. Small tubercles may be seen surrounding lesion. Usually many granulations	Fungous, rarely granulations, never entirely interstitial
Size	Smaller	Larger, but no regularity
Palpation	Ulcerated type: ragged undermined edges of the ulcer without diffuse infiltration. Edges often granular Papillomatous type: smooth surface, elastic, knobbed, glistening, no clearly defined limits	Roughened surface of usually stonelike character. Large fungous lesions have very hard base
Bleeding	Usually slight	Common, large amounts often
Discharge	Ulcerated type: greenish yellow, foul, purulent, slightly bloody Papillomatous type: mucoid in character, rarely bloody	Abundant, very fetid, watery, often bloody
Sensitiveness	Present	Usually absent
Pain	Slight or absent	Usually present and characteristic
Course	Papillomatous type: slow ulcerated type: also slow, but may produce fistulas or extensive ulceration	Faster, progressive, diagnostic symptoms
Histology	Characteristic tubercle formation with or without giant cells	Typical squamous-cell epithelioma with pearl formation
Age of onset	Twenty to forty years	Thirty-five to fifty years
Bacteria present	Tubercle bacillus, positive guinea pig test	Secondary invaders. No tubercle bacilli
Gram's iodine test	Negative	Positive

The only positive method of arriving at a diagnosis is to perform a biopsy and have a competent pathologist examine a specimen of the suspicious area of the cervix. The specimen of tissue must be of sufficient size to allow the pathologist to make a diagnosis. This section should include all constituents of the cervix. The biopsy will in no way injure the patient; the issues at stake are of such gravity as to make a correct diagnosis imperative. The earlier literature upon this subject is full of reports of cases in which biopsy was not used, and in which radical surgical procedures were performed for the eradication of a supposed carcinoma of the cervix, with the higher operative mortality and

morbidity, not to mention the anxiety that the false diagnosis of cervical carcinoma caused the patient and her relatives.

The differential diagnosis must distinguish this disease from hypertrophy with eversion and erosion of the cervix, myomatous or polypoid changes, actinomyces, syphilis, gonorrhea, sarcoma, and carcinoma. Biopsy will be of great aid in the differential diagnosis if it is considered together with the history, physical examination, and laboratory findings.

The treatment of this disease should be surgical whenever possible, and should be of a radical type if the condition of the patient will permit and if other factors are favorable. The contraindications for surgical treatment are advanced local tuberculous lesions, with involvement of neighboring structures, such as the rectum or bladder; tuberculous salpingitis; active tuberculosis elsewhere in the body; marked secondary infection; senility, and cardiovascular disease. The prognosis depends upon the type of treatment instituted, whether or not other tuberculous foci are present, and the state of their activity.

Beyea in 1901 reviewed the reports of 68 cases of tuberculosis of the portio vaginalis and cervix uteri, and added a case of his own. He demonstrated that radical surgical treatment gave the best prospect for a permanent cure. Fifteen of these patients were treated surgically. Seven of the 10 patients who were treated by panhysterectomy recovered completely. One patient who was treated by curettage, amputation of the cervix, and bilateral salpingo-oophorectomy was apparently free from tuberculosis sixteen months after operation. Eleven patients were treated conservatively with local applications (cauterization). One of the latter patients is said to have recovered; 5 were improved temporarily, and in the other 5 cases, the disease progressed. Brook, Moore, Spalding, Harris, Bishop and Murphy expressed the opinion that radical surgical treatment is the only safe means of giving the patient the greatest chance for a permanent cure and recommended either abdominal panhysterectomy or, in certain selected cases, a vaginal hysterectomy. Neu said that the use of dilatation and curettage was exceedingly dangerous in this disease because of the possibility of spreading the tuberculous process into a noninfected endometrium. In his experience cauterization was of little value. In the Berlin Medical Clinic, 55 patients were treated by radical surgery and 75 per cent were living and well five years later. Twenty-two other patients were treated by conservative measures and only 52 per cent were still living at the time of his report. Neu thus believed that radical surgical treatment was indicated in view of the poor prognosis offered by other measures. Wharton believed that surgical treatment should not be undertaken until it has been determined whether or not there is coexisting tuberculous salpingitis and endometritis; if these conditions are present, their extent and state of activity should be carefully noted before deciding on operation. Sasaki expressed the opinion that radium has a beneficial influence upon this disease, because it causes a specific rapid degeneration of the tuberculous tissue, and subsequent marked fibrosis develops. Davis said that panhysterectomy, performed either by the abdominal or the vaginal route, is the treatment of choice if the condition of the patient permits. He advised cauterization of the cervix before an abdominal panhysterectomy is performed. In his opinion, amputation of the cervix is a very questionable procedure; however, a few cures have been reported in the literature, by the employment of this procedure.

The following is a brief résumé of the salient features of the case that we wish to report:

#### REPORT OF A CASE

A nun, aged twenty-two years, registered at the clinic on June 25, 1934. The family history did not reveal carcinoma, tuberculosis, diabetes mellitus. Her father and mother, together with three brothers and four sisters, were all living and well. At the age of six years she had had an attack of sciatica. Three years before coming to the clinic, the patient had had an attack of plenrisy, which was of short duration.

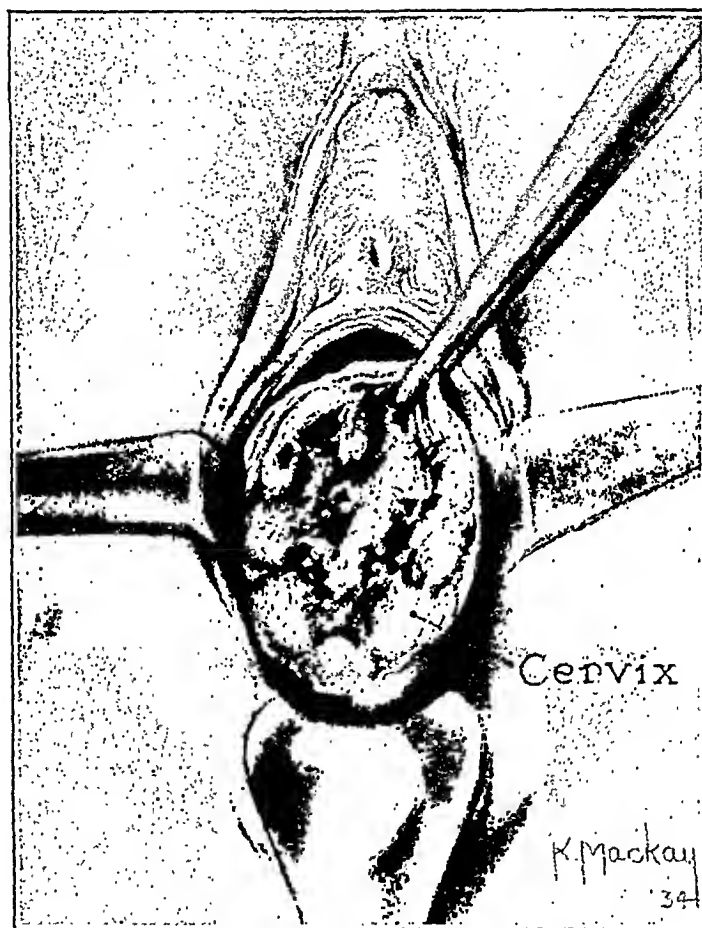


Fig. 1.—Tuberculosis of cervix.

An appendectomy had been performed elsewhere in 1921 for chronic appendicitis. Meneses had begun at the age of fourteen years and periods had occurred irregularly, from two to twelve weeks apart. The duration of the period had varied from five to seven days. Leucorrhea was present and was graded 3 upon a basis of 4. However, the menstrual periods had become "normal" during the past six months. The last menstrual period had occurred on May 23, 1934.

The present illness had appeared gradually three years ago, about six months after the appendectomy. This had been characterized by a sharp or a dull intermittent pain, which had been localized in the left lower quadrant of the abdomen. This had been made worse by a sudden motion and by menstruation. It had also been accompanied by a profuse foul, greenish yellow leucorrhea which required the constant wearing of a protecting sanitary napkin. She had been told elsewhere

that a tumor or an enlarged ovarian mass could be palpated in the lower part of the abdomen, for which surgical treatment had been urged. Aside from an occasional headache, the past history was otherwise normal.

Physical examination revealed that her height was 5 feet and 2 inches. She weighed 111 pounds; her average weight had been 112 pounds. Oral temperature was 99.6° F. The pulse rate was 90 per minute; the rhythm of the pulse was regular and the volume was good. Systolic blood pressure was 120 mm. and the diastolic was 80 mm. of mercury, respectively. Aside from moderately enlarged and chronically infected tonsils, the general physical examination was normal and revealed no abnormalities. Examination of the vagina and cervix with a speculum disclosed a marked hyperplasia of the cervical mucous membrane; this was firm and had a cauliflower-like appearance (Fig. 1). One portion of the lesion appeared to transverse the cervical canal and to present at the external os. There were several grayish plaques in this lesion. Biopsy was advised for diagnosis.

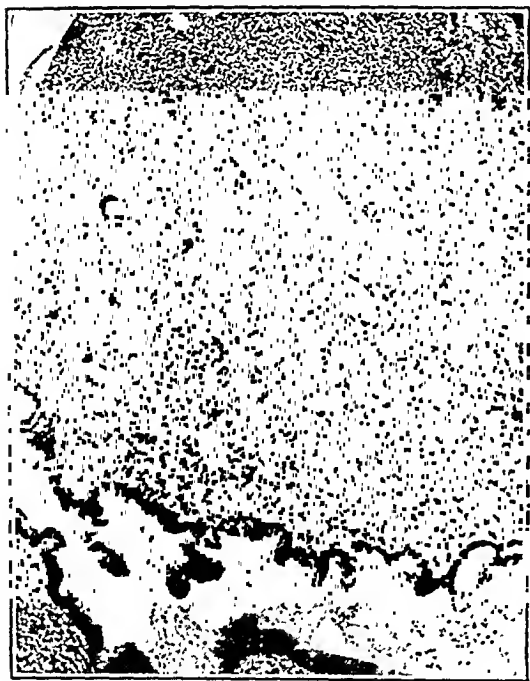


Fig. 2.

Fig. 2.—Tuberculosis of cervix uteri, showing typical giant cell and large collections of epithelioid and small lymphocytic cells ( $\times 65$ ).



Fig. 3.

Fig. 3.—Typical tubercle formation in cervix uteri ( $\times 120$ ).

The laboratory studies were as follows: The voided specimen of urine revealed an occasional erythrocyte and numerous leucocytes, which were graded 3 on the basis of 4. The value for the hemoglobin was 15.2 gm. per 100 c.c. of blood. There were 5,600 leucocytes per cubic millimeter of blood. The flocculation test was negative. Roentgenologic examination of the chest did not disclose anything abnormal.

On June 28, 1934 a biopsy of the cervix was done and the pelvis was examined while the patient was under anesthesia. The pelvic examination revealed the presence of a normal sized uterus and normal adnexa. Examination of the specimen, which was removed, revealed the presence of tuberculosis (Figs. 2 and 3). The lesion covered the entire external os and extended up the cervical canal. It was accompanied by a marked secondary infection, and it was believed advisable to cauterize the cervix thoroughly, and to observe whether or not the lesion healed as a result

of this treatment. If this failed to eradicate the disease, we intended to perform a total abdominal hysterectomy at a later date.

The postoperative convalescence was uneventful. On July 26, 1934 the patient was again examined under anesthesia. Examination of specimens, which were removed for biopsy at this time, revealed only inflamed granulation tissue and did not disclose any sign of the presence of tuberculosis. The pelvic examination also failed to reveal anything abnormal. The cauterized area had healed completely and the patient was dismissed from the hospital and went directly to her home fifty-three days after the extensive cauterization. During the last month of her stay in the hospital, she received sixteen applications of diathermy to the left lower quadrant of the abdomen to relieve a persistent dull pain in that area. The patient was advised to continue sanatorium regimen at home and to return to the clinic within four months for another examination of the cervix. A recent letter from her stated that her health had been greatly improved and that she had returned to her profession of teaching.

This is an undoubted example of the secondary type of tuberculosis of the cervix and probably originated from an attack of active pulmonary tuberculosis which manifested its presence by an attack of pleurisy three years ago.

#### SUMMARY

Tuberculosis of the cervix is very uncommon. Most cases are secondary infections, which are derived from primary foci elsewhere in the body. The literature on this subject has been partially reviewed. There are probably 300 cases which have been reported in the literature; of these, not more than 35 are primary tuberculous infections of the cervix. Biopsy is the only accurate method of diagnosing this lesion and of distinguishing it from cervical inflammations and carcinomas. Proper treatment appears usually to demand radical surgical procedures so as to insure the highest percentage of permanent cures. The only proved case of this disease which we have been able to find in our records is briefly reported.

#### REFERENCES

- (1) *Ajello, Abele*: *Riforma med.* 16: 615, 626, 639, 1900. (2) *Babés, M.*: *Bull. Soc. anat. de Par.* 58: 341, 1883. (3) *Beyea, H. D.*: *Am. J. M. Sc.* 122: 612, 1901. (4) *Bengolca, A. J., and Pavlowsky, A. J.*: *Semana méd.* 33: 1747, 1926. (5) *Berkeley, Comyns*: *J. Obst. & Gynec. Brit. Emp.* 3: 31, 1903. (6) *Bishop, E. L.*: *Am. J. Obst. & Gynec.* 19: 822, 1930. (7) *Boivin and Dugés*: Quoted by Williams, J. W. (8) *Bonnet, Louis, and Builliard, Henri*: *Gynéc. et Obst.* 24: 97, 1931. (9) *Brook, W. H. B.*: *J. Obst. & Gynec. Brit. Emp.* 3: 537, 1903. (10) *Cohnheim, Julius*: Quoted by Williams, J. W. (11) *Cornil*: Quoted by Williams, J. W. (12) *Croft, E. O.*: *J. Obst. & Gynec. Brit. Emp.* 1: 639, 1902. (13) *Culbertson, Carey*: *Surg. Gynec. Obst.* 38: 702, 1924. (14) *Cullen, T. S.*: *Surg. Gynec. Obst.* 22: 261, 1916. (15) *Daniel, C.*: *Gynéc. et obst.* 11: 161, 1925. (16) *Davis, C. H.*: *Gynecology and Obstetrics*, Hagerstown, Maryland, 1933, W. F. Prior Company, pp. 84, 85. (17) *Davis, J. E.*: *Am. J. Surg.* 17: 32, 1932. (18) *Derville*: Quoted by Williams, J. W. (19) *Douglas, Marion, and Ridlon, Magnus*: *Surg. Gynec. Obst.* 48: 408, 1929. (20) *Dworzak, Hans*: *Zentralbl. f. Gynäk.* 55: 2030, 1931. (21) *Emanuel, L.*: *Ztschr. f. Geburtsh. u. Gynäk.* 29: 135, 1894. (22) *Friedländer, C.*: Quoted by Williams, J. W. (23) *Geil*: Quoted by Williams, J. W. (24) *Greenberg, J. P.*: *Johns Hopkins Hosp. Rep.* 21: 97, 1920-1924. (25) *Gupta, N.*: *J. Obst. & Gynec. Brit. Emp.* 35: 334, 1928. (26) *Harris*,



B. A.: AM. J. OBST. & GYNEC. 20: 249, 1930. (27) *Horizontow, N. I.*: Zentralbl. f. Gynäk. 35: 1731, 1911. (28) *Horrocks, Peter*: Tr. Obst. Soc. London 44: 141, 1902. (29) *Kaufmann, Eduard*: Ztschr. f. Geburtsh. u. Gynäk. 37: 119, 1897. (30) *Kiwisch*: Quoted by Williams, J. W. (31) *Kroemer, P.*: Deutsche med. Wehnschr. 37: 1057, 1911. (32) *Kynoch, J. A. C.*: Brit. M. J. 2: 962, 1903. (33) *Labhardt, Alfred*: Ztschr. f. Geburtsh. u. Gynäk. 70: 532, 1912. (34) *Lancereaux and Lackerbauer*: Quoted by Williams, J. W. (35) *Lisfranc*: Quoted by Bonnet, Louis and Builliard, Henri. (36) *Lebert, H.*: Arch. f. Gynäk. 4: 457, 1872. (37) *Levers, A. H. N.*: J. Obst. & Gynec. Brit. Emp. 1: 632, 1902. (38) *Louis*: Quoted by Williams, J. W. (39) *Lukasiewicz*: Quoted by Williams, J. W. (40) *Mayor, A.*: Bull. Soc. anat. de Par. 56: 702, 1881. (41) *Meyer, Albert*: Arch. f. Gynäk. 45: 564, 1894. (42) *Moore, G. A.*: Surg. Gynec. Obst. 29: 1, 1919. (43) *Morgagni, G. B.*: De sedibus et causis morborum. Epistola 38, No. 34 (Ed. Radius) 1744. (44) *Murphy, J. B.*: Am. J. Obst. 49: 6, 1904. (45) *Neu, Maximilian*: Med. Klin. 7: 1223, 1911. (46) *Neuwirth, K.*: J. A. M. A. 81: 788, 1923. (47) *Norris, C. C.*: Gynecological and Obstetrical Tuberculosis, New York, 1921, D. Appleton and Company, 356 pp. (48) *Pavlovsky, A. J.*: Semana méd. 33: 611, 1926. (49) *Rokitansky*: Quoted by Williams, J. W. (50) *Sasaki, M.*: Oriental Med. 17: 79, 1932. (51) *Schlimpert, Hans*: Arch. f. Gynäk. 94: 863, 1911. (52) *Schmidt, H. R.*: Zentralbl. f. Gynäk. 50: 642, 1926. (53) *Schmorl and Birch-Hirschfeld*: Beitr. z. path. Anat. u. z. allg. Path. 9: 428, 1891. (54) *Sippel, Albert*: Deutsche med. Wehnschr. 20: 974, 1894. (55) *Spaeth*: Quoted by Williams, J. W. (56) *Spalding, A. B.*: Surg. Clin. N. Amer. 2: 351, 1922. (57) *Thiercelin, M.*: Bull. Soc. anat. de Par. 64: 313, 1889. (58) *Vassmer, W.*: Arch. f. Gynäk. 57: 301, 1899. (59) *Verneuil*: Quoted by Williams, J. W. (60) *Vineberg, H. H.*: Am. J. Obst. 57: 562, 1908. (61) *Virchow, Rudolph*: Virchow's Arch. f. path. Anat. u. Physiol. 5: 404, 1853. (62) *Watson, B. P.*: AM. J. OBST. & GYNEC. 27: 736, 1934. (63) *Weigert*: Quoted by Williams, J. W. (64) *Weigert, C.*: Deutsche med. Wehnschr. 23: 761, 780, 1897. (65) *Wharton, L. R.*: Surg. Gynec. Obst. 33: 145, 1921. (66) *White, Clifford*: Proc. Roy. Soc. Med. (Sec. Obst. and Gynec.) 23: 2, 1929. (67) *Williams, J. W.*: Johns Hopkins Hosp. Rep. 3: 85, 1893. (68) *Winters*: Discussion in Zentralbl. f. Gynäk. 11: 498, 1887. (69) *Zweigbaum, M.*: Zentralbl. f. Gynäk. 12: 494, 1888.

---

Orton, G. H.: X-Ray Treatment of Diseases of the Genito-Urinary System, Brit. M. J. 2: 343, 1934.

After discussing x-ray in the male genitourinary system, the author turns to a consideration of the female genital organs. In regard to carcinoma of the cervix, he feels that radiation therapy should not be done in any case where operation may be performed and that in those cases in which operation is contraindicated, the proper procedure is first to thoroughly irradiate the pelvis with x-ray, following this, six weeks to two months later, with radium. He feels that there are less recurrences with this form of treatment than when radium is first used. Carcinoma of the corpus is treated by operation if possible and if not by split doses of x-ray only. The same is said of ovarian malignancies. Menorrhagias due to nonmalignant conditions, and cases in which sterilization is desirable are discussed. Sterilization dose is considered to be 35 per cent of the skin erythema dose and the author uses 40 per cent, given either in one massive dose or divided into three or four small doses given at monthly intervals. Since small doses may stimulate ovarian function, one-tenth erythema dose is given in cases of sterility and amenorrhea and benefit obtained in about 25 per cent of cases. No deleterious effects have been found from this treatment. X-ray is also used in pruritus vulvae and leucoplakia, and the author feels that carcinoma of the vulva is best treated with combined x-ray and radium.

F. L. ADAIR AND W. G. BIRCH.

## THE METABOLISM OF LEVULOSE\*

### VII. THE INFLUENCE OF THE REPRODUCTIVE CYCLE ON TOLERANCE

ALLAN WINTER ROWE, PH.D., MARY A. McMANUS, A.B.,  
AND GERTRUDE A. RILEY, A.B., BOSTON, MASS.

*(From the Evans Memorial, Massachusetts Memorial Hospitals)*

IN PREVIOUS communications, certain general considerations bearing on the metabolism of levulose,<sup>21</sup> and the influences severally of hepatic dysfunction<sup>22</sup> and of the various levels of ovarian function<sup>23</sup> have been discussed. The present paper reports results obtained from the study of women during various phases of the reproductive cycle. The levulose investigations parallel in content and supplement an extended series in which pure galactose was used as the test sugar. These earlier data offer standards of usual performance with galactose in the several phases of reproduction,<sup>17</sup> and in the present group, galactose tolerances were measured as offering criteria for the functional normality of the carbohydrate metabolism in the subjects of the study. In addition to this simple procedure, each patient in the several groups was hospitalized and a comprehensive clinical and laboratory procedure, the "Long Form study," fully described elsewhere,<sup>18</sup> carried out in detail. By this approach, the normality of the individual subject became a matter of factual demonstration and not of opinion, a precaution the necessity of which has not always been recognized.

In determining the tolerance levels, the Hofmeister<sup>8</sup> technic of graded test meals to fasting subjects and examination of the urine for evidences of an exceeded assimilation limit has been adopted for reasons discussed at length in the earlier papers. The administration of the test meals in graded doses varying by 25 gm. has already been described.<sup>21</sup> The Benedict qualitative and Selivanov procedures have been used for the qualitative detection of the test sugar, while the combination of several technics involving the Benedict quantitative, Folin-Wu after clarifying with Lloyd's reagent, the precision polariscope, and the use of controlled fermentations with washed yeast have been applied to the quantitative estimation of the extent of the levulosuria. The full details of the several analytical procedures will be presented in a later communication. The basic data of the several component groups of the series are given in tabular form (Table I).

\*Presented at the Forty-sixth Annual Meeting of the American Physiological Society, New York City, March 30, 1934.

A brief description of each group is apposite. The antepartum section of the normal pregnant women were chiefly primiparas drawn largely from a home for unmarried mothers. An exception was a woman of forty-eight, studied at the end of the second month of her thirteenth uneventful pregnancy. Omitting this case, the ages ran

TABLE I. GROUP COMPOSITION

SUBGROUP		NO.
I	Pregnant, normal, antepartum	19
	Pregnant, normal, postpartum	12
II	Pregnant, toxic, antepartum	21
	Pregnant, toxic, postpartum	23
III	Abortion, postpartum	12
IV	Breast amputation	4
Total		91

from fifteen to twenty-three, with an average of twenty years. They were studied from the third to the ninth month of pregnancy, the average being between the sixth and seventh months. A number of these same patients appeared in the postpartum section, supplemented by others not examined before delivery. The examinations of the postpartum series were all carried out within a few weeks of the natural termination of gestation. The average age of the group was twenty-two years.

Group II, the toxic series, was composed of patients admitted to the Robinson Memorial presenting some one of the several toxemias of pregnancy. It was purposed to test them both before and after confinement, but for a variety of reasons this was possible with only a fraction of the group. These were older women, in all but six instances multiparas, and many of them presenting histories of one or more earlier toxic crises. The ages ranged from twenty to forty-four, the average age antepartum being thirty, and in the postpartum section, thirty-two years. The average parity was between four and five in each subgroup, the extremes severally being i and xiii. All stadia of pregnancy were represented from the second to the ninth month; the average was between six and seven months, or that shown by the normal group. All examinations postpartum were made within four weeks of the time of confinement.

The small group examined after abortion comprised both spontaneous and induced terminations of pregnancy. They ranged from para i to para vii, with an average of iii; the ages fell between twenty and thirty-five, with an average age of twenty-seven years. The duration of pregnancy before termination varied from six weeks (an ectopic pregnancy) to five months, the average here being a little less than three months.

The final group (IV), cases of breast amputation, was composed of four women who had had bilateral mastectomies for causes other than

malignant neoplasm. They were a still older group, as might be anticipated, the average age being forty-three years. The reason for their inclusion will be discussed later.

Spontaneous evidence of disturbed carbohydrate metabolism is offered by glycosuria where physiologic glycuuresis is ruled out. The urine sugar data are given in Table II.

TABLE II. GLYCOSURIA

GROUP		POSITIVE (%)
I	Antepartum	58*
	Postpartum	92†
II	Antepartum	16
	Postpartum	50
III	(Postpartum)	50
IV		0

\*Earlier studies 18% to 38%<sup>17</sup>

†Earlier studies 82% to 100%<sup>17</sup>

The incidence of glycosuria is definitely higher in the normal antepartum group than in any other series which we have studied. Our own values, in turn, are higher than the usual report<sup>7</sup> as we collected numerous specimens<sup>18</sup> from each patient and thus increased the probability of observing what is usually an irregularly intermittent occurrence. In the present series, the combination of a high carbohydrate intake by individuals with a physiologically lowered tolerance and living a sedentary life has probably produced a magnified glycucretic effect. Certainly, in none of the other data is there evidence of an abnormally low assimilation limit in this group either ante- or postpartum. In any case, the differences are those of degree. In the latter series (p.p.), the present figure is in harmony with the earlier records.

The toxic series, Group II, show a relatively low incidence of glycosuria antepartum, and one definitely so after delivery. These women were all toxic, and their food intake had certainly been low prior to admission. It is generally conceded that several days of liberal carbohydrate feeding should precede a tolerance test if the results are to be reasonably reliable. Soisalo<sup>25</sup> denies the need of this precaution when blood sugar curves are the indices.

The abortion group also shows a low incidence of glycosuria for the postpartum interval, but the brief duration of the pregnancy, in the majority of these cases, had certainly precluded the establishment of the low carbohydrate level that characterizes the later stadia of gestation. The present figure is to be regarded as wholly consistent with the individual existing conditions. The members of Group IV show no glycosuria, a result to be anticipated.

The blood sugar values for the series are collected in Table III.

But few comments need be made. In both Groups I and II the antepartum level is low, a condition characteristic of pregnancy. After delivery, the averages rise to levels both normal in themselves

TABLE III. BLOOD SUGAR

GROUP	SUGAR (MG.)		
	HIGH	LOW	AVERAGE
I Antepartum	108	77	87
Postpartum	—	—	94*
II Antepartum	105	70	85
Postpartum	114	81	92
III (Postpartum)	104	82	93
IV	100	83	95

\*Series record incomplete.

and comparing favorably with each other. The figures reported by one of us<sup>18</sup> from repeated studies on a considerable group studied throughout pregnancy and for a number of weeks postpartum are 83 and 94 mg., respectively. It will be noted further that the zone defined by the maximum and minimum values is not a wide one in any of the series, and the single minimum in the toxic group antepartum is the only value that can be regarded as significantly low. High values are conspicuously absent.

Before discussing the results obtained with the several study series, the criteria for normal performance should be considered, both for levulose and for galactose (Table IV).

TABLE IV. NORMAL STANDARDS

GALACTOSE	STADIUM	LEVULOSE*
20 gm.	Prepuberal	75 - 100 gm. (Av. 81 gm.)
20 - 40 gm.	Puberal (1st year)	75 - 100 gm. (Av. 89 gm.)
40 gm.	Adult	100 - 125 gm. (Av. 105 gm.)

\*Values are approximate.

With the latter sugar, the prepuberal child responds positively to a dose of 20 gm. and shows a progressive increase to 40 gm., the adult level, during the first year of the catamenia. With the former, as is shown in the table, there is no sharp line of demarcation between the prepuberal and puberal groups, although the average of the latter indicates an increase of modest proportions which is confirmed at a yet higher level in adult years. There is certainly an upward tendency here, but one relatively much less marked than in the case of galactose.

The data for the normal pregnant group are given in Table V.

TABLE V. NORMAL PREGNANCY

LEVULOSE TOLERANCE	PARTUM	
	ANTE-	POST-
High	100 gm.	150 gm.
Low	50 gm.	50 gm.
Average	68 gm.	77 gm.

Antepartum, the high level as observed is the lower value for the normal adult in a state of sexual rest. The majority of the group gave positive tests at absolutely lower levels, and the average is definitely below that of the prepuberal tolerance. After delivery, there is an irregular return toward earlier levels which in individual cases may even exceed the adult high normal. The average is still lower, however, than that of prepuberal years, although the difference is not of proportions significant in so small a series and one with so wide a scatter in the individual results.

Turning to the literature 9 investigators<sup>3-6, 9, 11, 13-15</sup> report a total of 217 individuals tested orally with 100 gm. of levulose of whom 180, or 83 per cent, gave a positive levulosuria. In the individual series, positive findings ranged from 20 per cent to 100 per cent of the test subjects. Van Creveld and Ladenius,<sup>26</sup> using test meals of from 40 to 60 gm., report 38 in a series of 60 as positive (63 per cent), and 9 more (15 per cent) as questionable. On the other hand, Schroeder,<sup>24</sup> using meals of 150 gm., found but 17 in 95 cases (18 per cent) to be positive and only 3 of these were strongly so. In another group of 132 patients "in various states due to pregnancy," he reports 22.7 per cent as giving positive response. This is an early paper (1905), and it seems probable that the chemical procedures may be responsible for the failure of his cases to respond to so massive a dose of sugar. The data from the other sources, particularly those of more recent date, are roughly in accord with our own findings.

Under the general caption of toxic pregnancy are assembled individuals with a rather wide variety of etiologic conditions. The patients studied in our series were certainly toxic, but from the fact that they were available for somewhat protracted investigation, cannot be regarded, in the main at least, as presenting conditions of marked gravity. Their data may be regarded as an extension of those deriving from the normal group, with, however, a superimposed abnormal condition which in itself might well influence the carbohydrate metabolism.

TABLE VI. TOXIC PREGNANCY

LEVULOSE TOLERANCE	PARTUM	
	ANTE-	POST-
High	75 gm.	150 gm.
Low	25 gm.	25 gm.
Average	61 gm.	65 gm.

Antepartum, the limiting values of the positive zone have moved downward one unit (25 gm.), but the average is not greatly inferior to that of the normal series. While many of the toxic patients exhibited a renal element, the blood and urine findings negative any significant loss of renal permeability. Further, the toxic group shows an average tolerance level below that of the normal series, which is

in accord with the blood and urine findings. It seems doubtful if the renal factor could have produced a significant upward shift in the apparent tolerance. After delivery, however, the upward tendency toward normal levels shown by the average is very slight, but the scatter of the individual observations is even greater than with the normal group. With the latter, the depressing agency was the pregnancy, and, with its termination, mechanisms seemingly were at once initiated to restore the carbohydrate metabolism to its normal non-pregnant level. In the toxic group, on the other hand, the pathologic factor was not at once relieved by delivery, and seemingly there remained sequelae from which the organism recovered more slowly. Where the toxemia had not produced permanent organic change, it could reasonably be expected that time would ultimately restore the tolerance to the normal nonpregnant level.

A survey of the galactose values in this series may be expository to the thesis. Depending on the period of the pregnancy, 30 or 20 gm. may be regarded as normal values antepartum. After delivery, there is a transitory further lowering to 10 gm. (mammary saturation?) with a rather prompt return to the 20 gm. level and later ultimate restoration to the normal adult dosage of 40 gm.; the normal values for the test period postpartum would be 10 or 20 gm. Fifteen of the group gave normal antepartum levels, six were depressed to 10 gm., and one showed a high level of 40. The average of the series, 19.5 gm., is slightly low as the group contained several early cases. After delivery, fourteen gave the expected response with 10 gm. and nine more with the yet normal 20 gm. Only two cases exceeded this value, both responding to 30 gm.; the average of 15.2 gm. is slightly, but not significantly, high for a group of tests within a month of delivery.

The group of interrupted pregnancies offers further data of possible significance to the major problem.

The women composing this series had all conceived and had completed, on the average, about three months of the gestational period. There can be but little question that the maternal organism adapts itself gradually to the new series of physiologic functions intrinsic in the primary condition. One of us has shown<sup>20</sup> that there is a relatively abrupt change in the previously normal respiratory metabolism in passing through a zone, the median of which is about twenty-five or twenty-six weeks before delivery. The sugar (galactose) tolerance, as already noted, shows a gradual decline. In our present group, therefore, we have a series of women in whom have been initiated the various mechanisms incident to their pregnancies, but which, in the main, have not continued to the zone in which they are confirmed and dominantly operative. Some of the pregnancies had terminated spontaneously, this fact implying a superimposed morbid agency, while in others the abortion had been induced.

Without exception, these cases were all tested within two weeks of the expulsion of the fetus. The highest value is that of the high normal adult, the lowest, one unit (25 gm.) higher than in normal pregnancy. The average, while significantly below the nonpregnant nor-

TABLE VII. GROUPS III AND IV

LEVULOSE TOLERANCE	ABORTION	BREAST AMPUTATION
High	125 gm.	125 gm.
Low	75 gm.	100 gm.
Average	89 gm.	113 gm.

mal, is equally remote from the normal pregnant figure. In other words, the tolerance for levulose here exhibits the depressing effect of early pregnancy, and warrants the inference that the agencies intrinsic in the physiologic status have been engendered but still fall short of their full and final influence. The results with galactose are conventionally normal to the condition with but a single exception. This woman had a purulent endometritis, and acute infective processes are known to lower the utilization capacity for galactose; the levulose level in this case was at 75 gm.

The mammary glands of the female normally possess a potential mechanism in which galactose is essentially involved. Lactation implies either the synthesis of galactose from circulating blood glucose or its selective withdrawal from the blood stream; further, it conditions the conjugation of the two hexoses to form lactose. That the mammary glands play a definite rôle in the metabolism of galactose has already been discussed<sup>17</sup> and documented. In the present study, a group of four women have been included, all of whom had had both breasts removed for chronic mastitis (malignant neoplasm usually lowers sugar tolerance). The levulose data on this small group are identical with those for normal intact women; all of them, equally, showed a galactose tolerance of 20 gm., a depression of 50 per cent from the adult standard. However levulose may be utilized by the organism, and this is a matter still of some obscurity, it is obvious that it plays no direct rôle in the function of lactation. Equally, the combined data may be adduced to support further the inference of a mammary factor in the metabolism of galactose.

#### DISCUSSION

While both of these sugars are utilized in the body and their intrinsic energy ultimately made available to the organism by final oxidation to carbon dioxide and water,<sup>1, 2</sup> it must be evident that there are certain significant differences in the several mechanisms of their metabolism. Both possess the basic and fundamental property of forming glycogen; the metabolism intermediate to this final result,



on the other hand, must involve not only chemical differences, as determined by variation in molecular structure, but seemingly also divergent response to various physiologic agencies.

If individual doses be indicated broadly as relatively increased, normal, or diminished, without attempting the precision of an arithmetical expression, a first approximate estimate may be made of the degree of correlation between the several indications of the two sugars. (Table VIII).

TABLE VIII. GALACTOSE AND LEVULOSE CORRELATIONS

GROUP		% AGREEMENT
I	Antepartum	67
	Postpartum	58
II	Antepartum	62
	Postpartum	55
III	(Postpartum)	67
IV		0

Recognizing that the indices are rough since the standards are necessarily flexible, there is yet a general trend of agreement in only two-thirds of the first three groups, coupled with a complete lack in the fourth, which, however, involved a highly specialized mechanism. The toxic and normal pregnant series show a definite agreement in the correlations before and after delivery, while Group III, although the component cases were studied postpartum, has already been found to agree more nearly with nonpregnant standards. Its better agreement, therefore, with the two antepartum series is consistent with the other data.

Pregnancy certainly lowers the utilization capacity of the organism for levulose, as it does for galactose and indeed, by implication, for glueose. This must be due to some general factor common to the sugars as a whole and intrinsic in the fact of pregnancy. That mammary function, operative certainly with galactose, is not the agent, would seem to be indicated by the results from those patients without these glands. Nurnberger<sup>12</sup> has recently postulated the presence of lowered hepatic function in advanced normal pregnancies. His criteria, like the majority of vital function tests, are no more than end-results common to a wide variety of seemingly independent causes. Kriss and Hirschhorn,<sup>10</sup> on the other hand, interpret the lowered carbohydrate metabolism of pregnancy, demonstrated on the basis of glucose tolerance alone, in terms of lowered activity of the Islands of Langerhans. Their comment that the normal state is regained in a few days after parturition is hard to reconcile with a wealth of contradictory observations from reliable sources.

It seems reasonable to say that the explanation of the phenomenon is not as simple as these writers would infer, and that the precise mechanism is yet to be identified.

For whatever causes and in whatever manners, the fact may be recorded that pregnancy lowers significantly, but not uniformly, the utilization capacity for levulose in human beings, and the effect in the majority of individuals is but slowly dissipated after delivery.

Equally, the mammary glands seemingly play no special part in the levulose cycle of utilization.

## REFERENCES

- (1) *Carpenter and Fox*: J. Nutrition 2: 389, 1930. (2) *Carpenter and Lee*: Am. J. Physiol. 102: 635, 1932. (3) *Falk and Hesky*: Ztschr. f. klin. Med. 71: 261, 1910. (4) *Gottschalk*: Ztschr. f. d. ges. exper. Med. 26: 34, 1922. (5) *Gottschalk and Strecker*: Klin. Wchnschr. 1: 2467, 1922. (6) *Hetyenyi and Liebmann*: Klin. Wchnschr. 1: 1204, 1922. (7) *Hirschfeld*: Berl. klin. Wchnschr. 47: 1053, 1910. (8) *Hofmeister*: Arch. f. exper. Path. u. Pharmacol. 25: 240, 1888. (9) *Jaeger*: Ztschr. f. Geburtsh. u. Gynäk. 74: 586, 1913. (10) *Kriss and Hirschhorn*: Wien. klin. Wchnschr. 46: 616, 1933. (11) *Neu and Keller*: Monatschr. f. Geburtsh. u. Gynäk. 38: 383, 1913. (12) *Nürnbergger*: Arch. Gynäk. 153: 1, 1933. (13) *Pfeiffer*: Inaug. Diss. Strassburg, 1913. (14) *Reichenstein*: Wien. klin. Wchnschr. 22: 1445, 1909. (15) *Reichenstein*: Wien. klin. Wchnschr. 24: 862, 1911. (16) *Rowe and McGuinness*: AM. J. OBST. & GYNEC. 16: 687, 1928. (17) *Rowe and McGuinness*: AM. J. OBST. & GYNEC. 17: 351, 1929. (18) *Rowe*: AM. J. OBST. & GYNEC. 21: 644, 1931. (19) *Rowe*: The Differential Diagnosis of Endocrine Disorders, Baltimore, 1932, Williams & Wilkins. (20) *Rowe and Boyd*: J. Nutrition 5: 551, 1932. (21) *Rowe, Plummer, and McManus*: Am. J. M. Sc. 186: 15, 1933. (22) *Rowe, McManus, and Plummer*: New England J. Med. 210: 1163, 1934. (23) *Rowe, McManus, and Plummer*: J. A. M. A. 104: 451, 1935. (24) *Schroeder*: Ztschr. f. Geburtsh. u. Gynäk. 56: 134, 1905. (25) *Soisalo*: Acta med. Scandinav. suppl. 34: 184, 1930. (26) *Van Creveld and Ladenius*: Ztschr. f. klin. Med. 107: 325, 1928.

80 EAST CONCORD STREET

## RUPTURED INTERSTITIAL PREGNANCY

MANDEL WEINSTEIN, M.D., LONG ISLAND CITY, N. Y.

(From the Surgical Service of St. John's Hospital)

INTERSTITIAL pregnancy is one occurring in that portion of the fallopian tube passing through the uterine muscle. Meyer<sup>1</sup> and Wynne<sup>2</sup> state that about ninety-one instances of interstitial pregnancy had been recorded up to 1917. At that time, they themselves reported a series of 304 cases of extrauterine pregnancies observed in the Johns Hopkins' wards and found only two interstitial pregnancies. Rosenthal<sup>3</sup> collected 1,324 cases of tubal pregnancy from the literature and found that only 3 per cent were of the interstitial type. Lequex<sup>2</sup> was able to collect 75 cases up to the year 1911. There is probably a maximum of 200 reported cases that will withstand critical analysis as to the accuracy of diagnosis.

If we are to believe the gonorrheal origin of ectopic pregnancy, the infrequency of the interstitial variety may be explained by the fact that there are fewer mucosal folds in the interstitial area, and therefore a lessened incidence of gonorrheal infection.

The diagnosis of interstitial pregnancy is a difficult one and rarely made. The symptoms before rupture may be identical with those of tubal pregnancy, namely, abdominal pain, nausea, and changes in the menstrual history. Acute hemorrhages due to the extraordinary vascularity of the site of implantation are more frequent with the interstitial than with any other type; in fact, such hemorrhages may be

fatal. Prolonged amenorrhea is more apt to precede rupture than a tubal pregnancy, and there may be an interruption of the normal menses up until the time of perforation.

Interstitial pregnancy may be confused with pregnancy in a rudimentary horn of the uterus, in which the round ligament is also located on the outer side of the sac. However, the diagnosis is nearly always made when the tube ruptures, and signs and symptoms of serious intraabdominal bleeding occur. In many instances even upon the operating table the diagnosis has been questioned. Many cases of so-called spontaneous rupture of the uterus may have been advanced interstitial pregnancies. In fact, one must bear in mind that spontaneous rupture of the uterus during pregnancy is almost an unheard of occurrence.

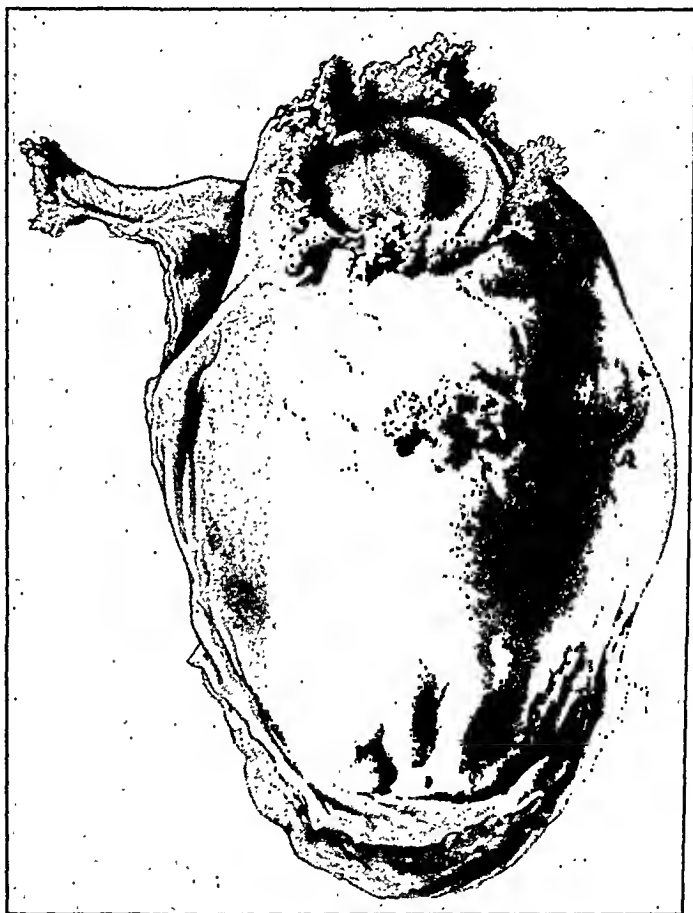


Fig. 1.—Specimen consisting of supracervical portion of uterus and gestation sac. Right tube is attached. Note projection of amniotic sac at superior larger site of rupture, and projection of chorionic villi at the smaller and inferior site of penetration. Also note difference in width of broad ligament stump in side of gestation sac as compared to broad ligament in the left.

The following case report is presented because of the great difficulty in distinguishing this type of advanced interstitial pregnancy from spontaneous rupture of the uterus. This diagnosis was made only following the examination of several specimens from portions of the tissue removed.

Mrs. L. P., aged thirty-eight years, married, housewife, was admitted to St. John's Long Island City Hospital, Oct. 19, 1933, at 3 P.M. with a diagnosis of ruptured ectopic pregnancy. In her history the chief complaint was abdominal pain, weakness, and a feeling of faintness. She had been married eleven and a half years

and never before had been pregnant. Concerning her surgical history, an appendectomy for chronic appendicitis had been performed twenty years previously. Venereal history was denied.

The menstrual history was negative, except that for the past eight years her periods have been irregular at times missing one, two, and three periods.

The last menstrual period occurred during the middle of July. She had noticed her breasts and her abdomen becoming larger. For the past two months patient had felt uncomfortable, tired, depressed, and a "gnawing feeling of hunger." Never experienced any weak spells, or fainting spells. No spotting, and no marked pain in either side of the abdomen.

About two days ago patient noticed pain in her right abdomen for the first time, transient in character. She felt faint, perspired a little. On the day of admission

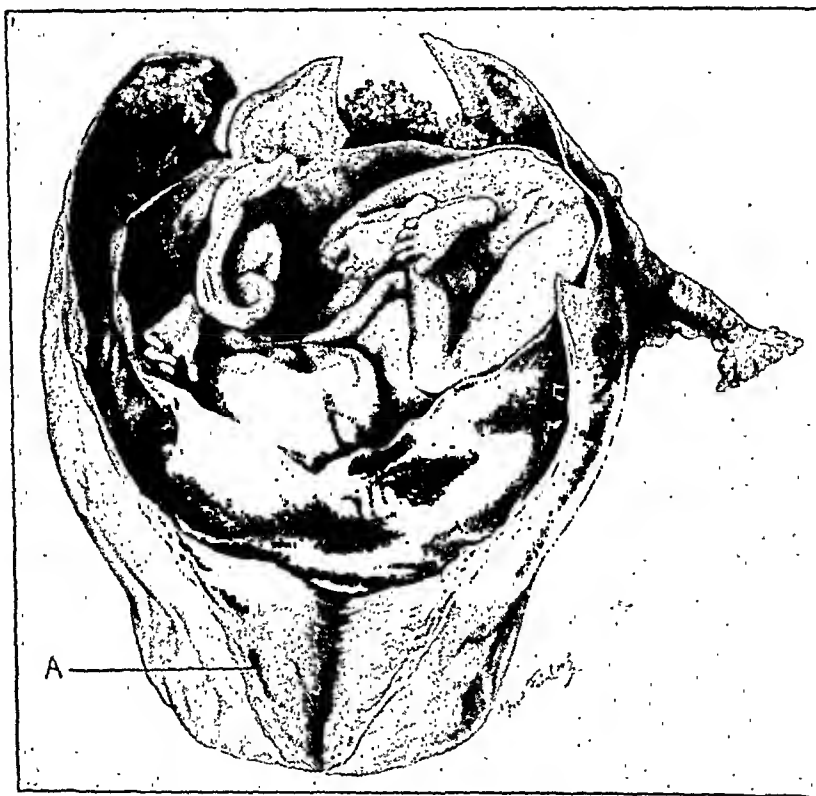


Fig. 2.—Gestation sac and uterus laid open. Note slitlike aperture of endometrial lumen in uterine body, which forms floor of gestation sac (A).

to hospital, she was unable to arise from her bed, due to severe abdominal pain and a feeling of faintness. She was getting fainter, perspired profusely, her feet and legs were cold, and eyesight dimmed.

On admission to the hospital her general appearance was that of a patient in profound shock; marked pallor of mucous membranes and cyanotic tinge to skin. Abdomen was distended slightly; a distinct fluid wave was elicited; there was dullness in the flanks; there were indefinite masses involving the whole lower abdomen, the summit of which reached to a point between the pubes and the umbilicus. Patient was cold, restless, pulse barely perceptible.

*Diagnosis.*—Ruptured ectopic pregnancy with extensive intraabdominal bleeding.

Patient received an intravenous infusion of 5 per cent glucose, followed by a transfusion of whole blood begun through the cannula.

*Operation.*—Incision: midline from symphysis to umbilicus. Large amount free and clotted blood in peritoneal cavity. Uterine and tubal mass, soft, enlarged to the size of a three to four months' pregnancy. There was a large perforation of

anterior surface of uterine tumor near the summit, through which the fetal sac protruded. A loose irregular placenta presented itself. Around the rim of this opening, there was active bleeding from lacerated veins along the margin of the perfora-



Fig. 3.—Section taken through uterine body; note slitlike lumen. A, Decidual reaction of compaeta; B and C, artifical separation from D spingiosa in which the charaeteristic hypertrophie glands of pregnaney are seen.

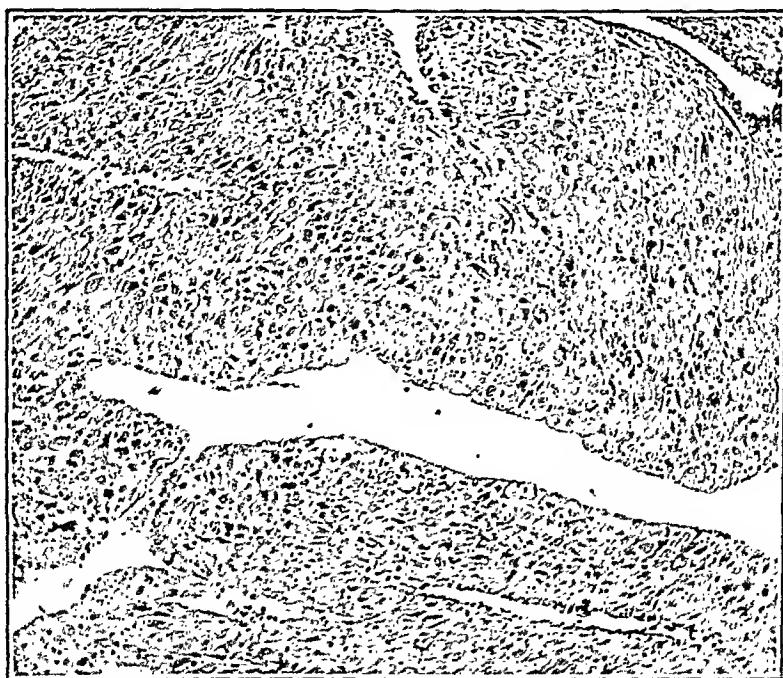


Fig. 4.—High power vlew of compaeta showing characteristic decidual cells.

tion. Placenta projected through anterior uterine wall and several other points. The anterior uterine wall was greatly thinned out and large veins were apparent beneath the serosa.

A rapid supracervical hysterectomy was done, together with the removal of the right tube which was included to save time in the dissection. One suture was used to bring the round ligament pedicles down to the cervix and to approximate bladder to posterior cervical aspect.

Throughout the operation 1,000 c.c. of whole blood were administered intravenously by means of the Hendon cannula.

Anesthesia was gas oxygen with a very small amount of ether added. Total time of operation about thirty minutes.

*Pathologic Report.*—(Dr. Jacob Werne.) Specimen was a uterus with right tube attached, the major portion of the structure being occupied by sac containing fetus and membranes. The long axis of the structure, 15 cm., formed an angle of about 45 degrees with a perpendicular erected from the supracervical stump, which made up the inferior pole of the specimen. The uterine body itself measured 5 cm. in length.



Fig. 5.—Section through gestation sac near site of rupture. A, Chorionic villi; B, fibrin and blood clot; C, attenuated wall of gestation sac. Note absence of decidual reaction.

Projecting from two sites of rupture,  $\frac{1}{2}$  and  $3\frac{1}{2}$  cm. in length, were fringes of chorion. The placental attachment over the posterior and superior aspect of the interior of the sac, which occupied over two-thirds of the volume of the specimen, had a diameter of 8 cm. Umbilical cord measured 15 cm. The fetus weighed 140 gm. (hardened specimen). Computed age, four and one-half months.

The uterine fundus, which formed the floor of the sac, had a thickness of 2 cm. Endometrium measured from 2 to 3 mm. in the gross; uterine lumen was distinct, slitlike. On the right, the broad ligament measured 10 cm.; on the left, 4 cm. The right tube was natural for a distance of 7 cm. from its patent fimbriated end to the point where its lumen was apparently closed and its wall continuous with the attenuated wall of the sac enclosing the fetus and membranes.

*Microscopic Examination.*—The compact layer of the decidua which replaced the normal endometrium was made up of characteristic large cells, oval and polygonal with large lightly staining vesicular nuclei. The underlying spongy layer contained

some moderately hyperplastic and dilated uterine glands, some of which extended for varying distances into the subjacent muscle. No chorionic villi were in evidence.

The gestation sac was exceedingly thinned, largely fibrous structure in parts hemorrhagic and necrotic. The attenuated portions showed chorionic villi invading the wall without intervening decidual reaction. Tubal wall (beyond site of gestation sac) was essentially natural.

Patient was returned to bed much improved. Her pulse dropped from 140 to 110, of better quality. Extreme pallor and cyanosis were now gone; mucous membranes were regaining their natural color. Restlessness, and all the previous symptoms of shock from hemorrhage, were rapidly disappearing.

The patient remained in the hospital until November 10. Throughout her stay she was fairly comfortable except for a mild attack of pleurisy in her right lower chest. This subsided readily and the patient was discharged November 10, on the twenty-second postoperative day. She had been seen several times during the months following her discharge from the hospital. Her health had been good, and she had regained the strength she enjoyed prior to her illness. The wound was thoroughly healed and presented a narrow scar. There were no complaints.

#### REFERENCES

- (1) *Ash, J. E.*: Gynec. & Obst. 54: 930, 1932. (2) *Leques*: L'obst. 4: 493, 1911. (3) *Miller, C. Jeff*: An Introduction to Gynecology, St. Louis, 1931. The C. V. Mosby Co. (4) *Meyer, A. W.*: Surg. Gynec. Obst. 28: 293, 1919. (5) *Rosenthal*: Zentralbl. f. Gynäk. 20: 1297, 1896. (6) *Schenone, Alfred A.*: AM. J. OBST. & GYNEC. 26: 904, 1933. (7) *Wynne, H. M.*: Bull. Johns Hopkins Hosp. 30: 15, 1919.

3064 THIRTY-SEVENTH STREET

## EMBRYONAL CYSTS OF THE CERVIX AND THEIR ETIOLOGY WITH A REPORT OF TWO CASES\*

J. KOTZ, M.D., F.A.C.S., WASHINGTON, D. C.

(From the Department of Gynecology and Obstetrics at George Washington University)

**L**ARGE cysts in the region of the cervix are extremely rare. The usual type of cervical cyst described is the nabothian cyst, which only exceptionally attains any great size. Cysts derived from congenital rests or malformations do not occupy a prominent place in the literature.

My object in presenting these two extremely interesting cases is, therefore, manifold:

1. The condition is unusual and rare. A thorough review of the literature, from 1890 up to the present, reveals, in all, about ten cases.

2. In no previous report is there any mention of what may or may not be an important coincidence, the fact that in both these cases, the condition arose during pregnancy and was primarily noted during labor.

3. The method of diagnosis employed is worthy of additional consideration.

4. The technic of removal is a principle applied for the first time to a cyst of this size, location, and character.

\*Presented at a meeting of the Washington Gynecological Society. November 24, 1934.

CASE 1.—Mrs. M. B., a housewife, aged thirty-two, presented herself at my office on Aug. 22, 1932 for routine prenatal examination and care. Her last menstrual period was March 14, 1932, and the estimated duration of her pregnancy about five months. Her past history was entirely negative, and general physical examination revealed no abnormalities. Pelvic examination showed a moderately relaxed perineum with moderate rectocele and cystocele. No evidence of cervical cyst existed at this time.

The course of pregnancy was uneventful. On Jan. 16, 1933, she went into labor. At about the end of the first stage of labor, I noted a small mass about the size of a walnut protruding from the vagina. This could be traced upward underneath the bladder as far as an examining finger could reach, and was firmly attached to the anterior lip of the cervix. The mass was pinkish, smooth, soft, not tender. Further examination was deferred as labor was not impeded by the presence of this mass.

I examined her six weeks later at my office. At that time the mass had doubled in size, although its general appearance was otherwise unchanged. The anterior

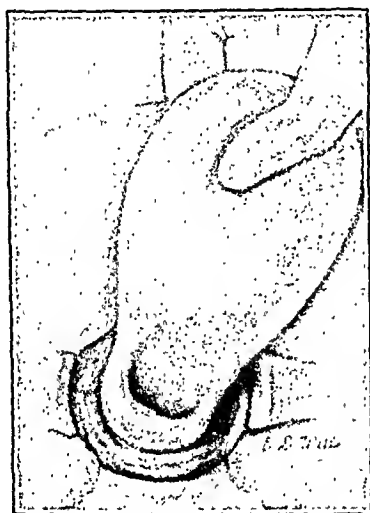


Fig. 1.

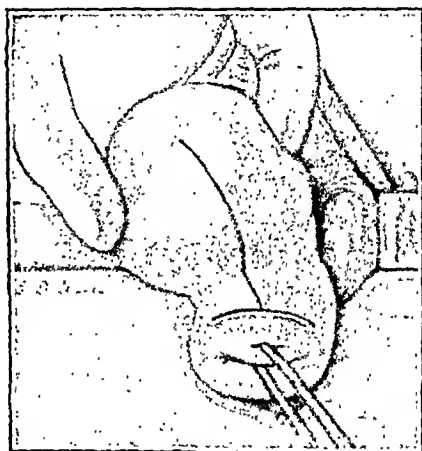


Fig. 2.

Fig. 1.—Posterior view of cyst showing its relationship to anterior lip of cervix.

Fig. 2.—First step of operation: T-shaped incision in vaginal mucosa.

lip of the cervix was about five times as long as the posterior and considerably thickened. Operation was advised but refused. Six weeks later, the patient now noticed the mass would protrude on standing and had grown to about the size of a medium-sized orange. I did not see this patient for about two years. The mass, in the meantime, had grown to proportions that no longer permitted it to prolapse, and the patient had begun to believe herself cured.

On May 25, 1934 she called by phone and told me that during the course of her morning housework, she had felt a sudden gush of fluid from the vagina. The fluid was thick yellow, with a very foul odor, and the amount lost was approximately a cupful. Later, at the office, about a cupful more of the same fluid exuded. Immediate operation was advised and this time accepted.

At the hospital, the patient was first examined under anesthesia. The mass was about the size of a medium-sized orange. It arose from the anterior lip of the cervix near its junction with the vaginal mucosa and extended upward underneath the bladder (Fig. 1). We were unable to determine its exact extent until x-ray study was made. The mass was bluish in color, smooth, soft, painless. A small perforation on the left exuded the same yellow fluid on pressure.



The perforation was closed off with a purse-string suture. The contents of the cyst were then removed with a large needle and syringe, and with the needle in place, lipiodol was injected, refilling the cyst. X-rays were then taken, and revealed the extension of the cyst upward in the general direction of the broad ligament. A metal catheter inserted in the urethra could be palpated at the base of the bladder above the cyst, and proved there was no connection between the two.

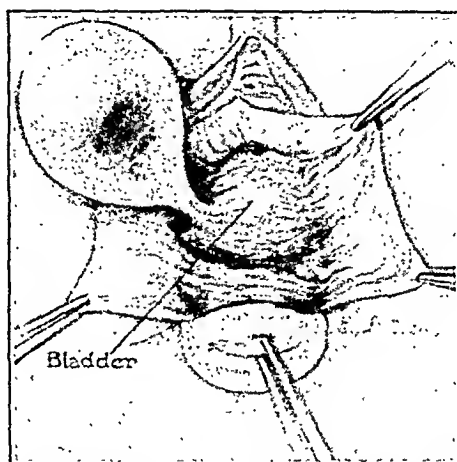


Fig. 3.—Cyst separated by blunt and sharp dissection.



Fig. 4.—Microscopic appearance of cyst wall, showing squamous epithelium resting on intact basement membrane.

The method of removal utilized a principle first described by Auster in March, 1933, for the excision of Bartholinian cysts following paraffin injection. The lipiodol was first withdrawn and hot paraffin wax injected to fill up the cyst. This was allowed to harden. An inverted T-shaped incision was then made in the vaginal mucosa similar to that used in the repair of a cystocele (Fig. 2). The mucosa was denuded on both sides by blunt dissection, gradually exposing and delivering the cyst (Fig. 3). The cyst was easily shelled out; the pedicle, which was found rather high up and attached between the layers of the broad ligament, was ligated

and cut. The vaginal mucosa was then brought together with continuous No. 2 chromic catgut suture.

Microscopic examination revealed sections of a cyst wall lined with a smooth hyperplastic layer of squamous epithelium resting on an intact basement membrane. The stroma was infiltrated with lymphocytes and plasma cells. No evidence of malignancy was present (Fig. 4).

The patient made an uneventful recovery and her condition at the present time is good.

CASE 2.—Mrs. C. K., aged thirty, housewife, runs almost a parallel course except that the cyst was removed about two months after its discovery—this operation being performed at the time of delivery. Her recovery was uneventful. Histologically, the picture revealed a cyst lined by simple cuboidal epithelium which in areas had undergone a pressure atrophy. The epithelium rested on an intact basement membrane. The remainder of the cyst wall was smooth muscle and fibrous connective tissue and many thin-walled, dilated blood vessels. No evidence of malignancy or recent inflammatory reaction was seen (Fig. 5).

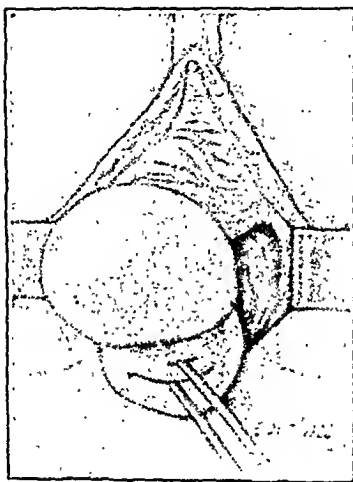


Fig. 5.—Gross-appearance of Gaertner's duct cyst, anterior view, Case 2.

In my opinion, these cysts arose from patent Gaertner's ducts in the anterior cervical wall. Nabothian cysts are generally much smaller and arise by occlusion of a cervical gland duct due to a chronic endocervical inflammatory process, and are the result of a congenital anomaly. A cyst arising from an incomplete fusion of the müllerian ducts is eliminated as a possibility because of the absence of a double vagina and uterus. Again, a cyst formed by the protrusion of a supernumerary ureter into the lateral vaginal wall would show the typical microscopic picture of a ureter.

#### REFERENCES

- (1) *Auster, L.*: Am. J. Surg., p. 509, 1933. (2) *Frank*: Gynecological and Obstetrical Monographs, New York, 1922, D. Appleton-Century Co. (3) *Kelly, Howard*: Gynecology, New York, 1928, D. Appleton-Century Co. (4) *Skene, A. J. C.*: Med. Rec. 49: 692, 1896. (5) *Suss, J.*: Zentralbl. f. Gynäk. 47: 71, 1923. (6) *Tarsia*: Zentralbl. f. Gynäk. 31: 209, 1907. (7) *Unterberger*: Monatschr. f. Geburtsh. u. Gynäk. 29: 587, 1909. (8) *Warren*: Tr. Maine Med. Assn. 8: 115, 1883. (9) *Young*: Boston M. & S. J. 152: 216, 1905.

1835 EYE STREET, N. W.

## INTRAUTERINE GAS GANGRENE WITH RECOVERY

WILLIAM D. CARRELL, M.D., TUCSON, ARIZ.

THIS case is of particular interest because of the recovery with a method of treatment, which violated one of the fundamental rules of the handling of gas gangrene infections in general. The early removal of diseased tissue was purposely neglected due to the site of infection, and was without doubt one of the greatest factors in aiding recovery. The treatment given was quite conservative and could be followed even in the home.

Mrs. B. D., white, female, aged twenty-nine years, admitted to the Southern Methodist Hospital Jan. 27, 1935. A previous diagnosis was made of an active pulmonary tuberculosis in the right apex, and a pregnancy of four months' duration. Two days before admission, she began complaints of severe headaches, blurring of vision and spots before the eyes, nausea, and vomiting. The blood pressure was found to be 240/150, and her eyegrounds showed definite choked discs. At the time of admission she had a slight vaginal discharge of blood. Therapeutic abortion was recommended by the referring physician. No uterine cramps were present.

She had been married ten years, having four children, aged eight, six, four, and two years. Her husband had had pulmonary tuberculosis for several years. In November, 1933, she had an hemoptysis and was in bed four days. About one year ago a diagnosis of pulmonary tuberculosis was made by x-ray plate. In May, June, and July, 1934, she was in St. Mary's Hospital because of her tuberculosis. While a patient there, she induced an abortion with a "slippery elm stick" and was curetted. In November, 1934, she had a pulmonary hemorrhage and was sent to the County Hospital, where she remained until transferred to the Southern Methodist Hospital. She was having no cough or expectoration. Her weight in November, 1934, was 101 pounds and in January, 1935, was 110 pounds. Appetite good, bowels regular, no indigestion. Slow expulsion of urine, no dysuria. For the past two months she had urinated twice daily, but large amount passed each time. Last menses, Aug. 26, 1934.

Examination revealed a moderately undernourished white female. Abdomen negative, except that the fundus of the uterus was halfway between the symphysis pubis and the umbilicus. The cervical canal was patent, and there was a discharge of a small amount of brownish blood having a foul odor. On Jan. 29, 1935, the urine had a specific gravity of 1.024 and contained a large amount of albumin, an enormous number of red blood cells in the uncentrifuged specimen, a few hyaline, and an occasional granular cast.

On Jan. 27, 1935, with aseptic precautions, the vagina was packed tightly around the cervix with wet cotton pledgets. She was given 20 c.c. of 10 per cent magnesium sulphate intravenously and two ounces of magnesium sulphate solution by mouth. Her temperature did not exceed 99° during the next two days. On Jan. 29, 1935, at 9:00 A.M. the vaginal packing was removed. The cervix was found to be soft and slightly dilated. The cervix was further dilated with a Goodell dilator and a piece of gauze was packed very loosely in the cervical canal. At this time she had had no uterine contractions. The blood pressure was 198/124 and the pulse rate 100. She was given a second 10 c.c. of 10 per cent magnesium sulphate solution intravenously. At 8:00 P.M. on this date she had a chill, followed shortly by a second chill. The gauze packing was removed and obstetrical pituitrin two minims hypodermically every thirty minutes was ordered. At 10:00 P.M. the temperature

was 105.6°, the pulse 140 per minute, weak and thready. Digifoline, 2 c.c. hypodermically every three hours, was ordered for four doses. She was having a few uterine cramps at this time. The next morning the temperature was 98.6° and the pulse rate was 106. At 2:00 P.M., Jan. 30, 1935, she was having severe cramps, and I was called to the hospital because the nurse felt that the fetus would soon deliver. Her temperature at this time was 101.6° and the pulse was 126. She was taken to the delivery room and prepared for a vaginal examination. The cervix was plugged with a clot but admitted two fingers, at which time there was expelled from the uterus a large amount of gas with a fetid odor. Smears from the bloody discharge following the gas showed enormous numbers of gram-positive, encapsulated, rodlike bacilli, typical of the Welch bacillus. She was immediately put under quarantine and given intravenously one therapeutic dose of polyvalent gas gangrene antitoxin (Lederle) containing 10,000 units of *Perfringens* antitoxin, 10,000 units *Vibrio* Septique antitoxin, 200 units *Oedematiens* (Novyi) antitoxin, 200 units *Sordellii* antitoxin, and 25 units *Histolyticus* antitoxin. At 6:00 P.M. the fetus delivered spontaneously. It was very badly macerated and could be identified as a fetus only by the skeletal tissue. The soft tissues were full of gas. Moderate manual pressure on the fundus uteri did not expel the placenta. A second dose of the serum was given intravenously at this time. At 2:00 A.M., Jan. 31, 1935, the third dose of serum was given intravenously, and again at this time the placenta could not be expelled by pressure on the fundus. At 10:00 A.M. the placenta could not be expressed. There was less gas from the uterus. The fourth dose of serum was given intravenously. Later, on this day, we obtained from the patient the admission that on two occasions, shortly before she was admitted to the Southern Methodist Hospital, she passed a "slippery elm stick" into the uterus in order to induce an abortion. At 6:00 P.M., the fifth dose of serum was given intravenously, and the placenta could not be expressed. At 8:30 A.M., Feb. 1, 1935, a direct blood transfusion of 400 c.c. was given, followed by the sixth dose of serum intravenously. The placenta was then removed by gently stripping it loose from the uterine wall with two fingers inserted through the vagina while pressure was applied to the fundus through the anterior abdominal wall. The portion of the placenta attached to the fundus was firm and in good condition, but the loose lower portion was filled with gas and was gangrenous. She had a severe chill for twenty minutes, following the transfusion, and the temperature went up to 103.6°, the highest temperature for the preceding twenty-four hours having been 99.4°. The temperature dropped to 98.6° at 4:00 P.M. On February 2 there was no serum available in Tucson. The patient was much improved, ate well, and the highest temperature this day was 100.6°, and the pulse rate was 90 and of good quality. A small amount of gas escaped from the vagina when pressure was applied to the fundus uteri. On February 3 the patient showed further improvement, and no gas could be obtained from the uterus. The seventh dose of serum was given on this day. She continued to run a low-grade fever with a pulse rate of 70 to 80, until discharged on Feb. 10, 1935. On February 6 her blood pressure was 176/126. On this date she was referred back to the medical service. On February 8 a voided specimen of urine had specific gravity 1.020, trace of albumin, a few red blood cells, no casts, and a few pus cells. Cultures of the organism were not made, and the diseased tissue was not sent to the laboratory.

Several plans of treatment were considered. The patient was an extremely poor surgical risk. Hysterectomy would have been hazardous, due to the shock alone, and the added danger of infecting the peritoneal cavity with a following widespread gas infection caused such treatment to be discarded. The cervix was soft and open, and the uterine cramps suggested expulsion of at least the fetus soon after the type of infection was discovered. The fetus was expelled four hours after the diagnosis was made, but the entire placenta was retained and could not be ex-

pressed with moderate pressure over the fundus uteri. At this time she had received two doses of antitoxin, and the temperature was lower, but she was very weak and showed signs of rapid destruction of red blood cells. She was yet not a good surgical risk, and there was no evidence of spread of the infection. It was, therefore, decided to give more antitoxin in an effort to build up her immunity and to remove the placenta at a later date. On the third day after the onset of the symptoms of the infection and following a blood transfusion and the fifth dose of antitoxin, the uterus was manually cleaned, using no instruments in order to avoid spreading the infection further into the uterine walls and the blood stream. The intrauterine infection subsided rapidly thereafter, and with but two more doses of antitoxin she recovered.

It was felt that a gas gangrene infection within the uterine cavity would be less likely to spread than in almost any other space in the body. Treatment was aimed at building up the general resistance to the infection, doing as little as possible to initiate its spread by surgical intervention.

123 SOUTH STONE AVENUE

---

## THE DETERMINATION OF RUPTURE OF THE MEMBRANES

ARTHUR G. KING, M.D., M.Sc., CINCINNATI, OHIO

*(From the Department of Obstetrics, Methodist Episcopal Hospital, Brooklyn)*

WHETHER or not the fetal membranes have ruptured may at times be a question of great importance to the obstetrician. The history as given by the patient is often untrustworthy. In many cases the amount of fluid lost with the rupture is so slight as to escape detection in the ordinary nursing care. The determination by a vaginal examination is not always easy and this procedure is not considered entirely harmless by all authorities. Hence, some other means of obtaining the information should be a valuable aid in obstetric diagnosis.

When the fetal membranes rupture, the alkaline amniotic fluid reduces the normal vaginal acidity to a neutral or faintly alkaline reaction. The detection of this alteration by an indicator dye would show that the bag of waters was no longer intact.

The use of litmus paper is not satisfactory because of a 35 per cent error due partly to the difficulty in reading the reaction and partly to the pH value at which the litmus color change occurs.

Using colorimetric methods, Temesvary<sup>1</sup> found the following pH values: amniotic fluid, 7.0-7.7; the vagina of pregnant women at term, 5.2-6.0; the vagina of women in labor with ruptured membranes, 6.0-8.1. These figures were confirmed by Bock<sup>2</sup> using the hydrogen ion electrode, the comparable values being: 7.1-7.7; 5.2-6.0; and 6.8-8.2.

Bromthymol blue changes very sharply from orange to blue green at a pH of 6.0-7.6. Temesvary used strips of filter paper soaked in a 0.2 per cent alcoholic solution, which, rolled up in gauze, were introduced into the vagina of 138 women. Clinical findings supported the test readings in 131 cases (73 intact and 58 ruptured membranes). The test failed in only 5 per cent of cases. Temesvary's pupil, Berling,<sup>3</sup> applied the test in 50 cases, reporting no errors.

This work presents a simple modification of the technic and the results in 314 cases. The indicator dye, dibromthymolsulphonphthalein, commercially known as bromthymol blue, is easily and cheaply obtainable. It is dissolved in either absolute or ordinary 95 per cent ethyl alcohol to make up a solution of 0.2 per cent strength. Well-made cotton applicators are dipped in the solution, allowed to dry, and then sterilized in glass jars by autoclaving.

To perform the test, the labia are separated and the applicator introduced well into the vagina and allowed to remain for a full minute. Urinary contamination need not be feared as the parturient woman's urine is almost invariably slightly acid. On withdrawal, the applicator, although sometimes covered with a little mucus, is easily "read." The original orange color indicates intact membranes; a change to blue green or the appearance of flecks of green anywhere indicates ruptured membranes. If the mucus is considerable, the applicator may be rinsed briefly in running water without affecting the reading. If mercurochrome has previously been instilled in the vagina, the test may still be used although it is a little harder to detect slight changes, and the mercurochrome-stained mucus must be washed off. It is important that the applicator remain in the vagina at least a minute, and occasionally the color change does not occur till several minutes after it is withdrawn.

The accuracy of the test is high. In 141 cases where the membranes were intact the test was negative 140 times (99.3 per cent). The one false positive response was in a bleeding case, and blood, of course, is slightly alkaline. Of 169 cases with ruptured membranes it was positive 160 times (94.7 per cent). The 9 false negatives may be explained by an insufficient amount of amniotic fluid: either all the water had drained off or the head had settled so as to prevent any further flow; as time passed, the natural acidity of the vagina reasserted itself and the test was therefore negative. An analysis of the percentage error in relation to the number of hours since rupture, where this was known, is given in the table. It shows that the accuracy decreases with the passage of time.

PERCENTAGE ERROR IN POSITIVE REACTIONS

HOURS SINCE RUPTURE	0-4 HR.	4-8 HR.	8-12 HR.	12-24 HR.	OVER 24 HR.
Positive readings	96	23	16	11	3
Falsely negative	2	1	1	1	4
Percentage error	2%	4%	6%	8%	57%

To record the accuracy of the test from the point of view of the interpretation of the reading, the following data are available: Of 161 positive readings the membranes were definitely ruptured in 160 (99 per cent). Of 149 negative reports the membranes were ruptured in 9 and intact in 140 cases (94 per cent).

In addition to the false positive test in the presence of free bleeding mentioned above, there were two positive readings that deserve comment. In one case a history of rupture several hours previously was obtained from the nurses' notes, but on a subsequent vaginal examination a thin sac was found. It was the amnion only and it ruptured at the first touch of the finger. The other case was identical except that the time of rupture could not be ascertained although amniotic fluid had been observed trickling. It is known that occasionally the chorion only may rupture with the discharge of a little fluid. In two other cases of the series negative readings were obtained but no history of the rupture of the membranes either before or after was recorded.

#### SUMMARY

1. The admixture of alkaline amniotic fluid to the normally acid vaginal secretions changes the reaction in the vagina. The resultant pH may be indicated by bromthymol blue which is exceedingly sensitive, and the dye may be used to determine whether or not the membranes are intact.

2. A simple technique is presented which employs sterile applicators dipped in a 0.2 per cent alcoholic solution and the results are easily read: an orange color indicates intact membranes, a bluish green, ruptured membranes.

3. The experiment involved 314 women. The test was accurate in 99 per cent of cases of intact membranes and 95 per cent cases of ruptured membranes. The cause of the single false positive reading and the 9 (6 per cent) incorrect negative readings is suggested.

4. The percentage error with ruptured membranes increases with the elapse of time following rupture: from 2 per cent within four hours through 8 per cent in from twelve to twenty-four hours, to over 50 per cent after twenty-four hours.

5. The test is likely to be positive in the presence of free bleeding and in the rare case where but one of the two enveloping membranes has ruptured.

#### REFERENCES

- (1) *Temesvary, N.*: Zentralbl. f. Gynäk. 57: 1180, 1933. (2) *Bock, A.*: Arch. f. Gynäk. 155: 444, 1934. (3) *Berlind, M. M.*: AM. J. OBST. AND GYNEC. 24: 918, 1932.

3236 BURNET AVENUE

# THE PREVENTION OF EXCORIATION OF THE PERINEUM FROM SILVER WIRE SUTURES\*

HERMAN GRAD, M.D., F.A.C.S., NEW YORK, N. Y.

*(From the Woman's Hospital)*

MANY years of use of silver wire sutures in the repair of complete laceration of the perineum has convinced me that in the majority of cases the silver wire suture causes considerable suffering. The pain arises, contrary to expectation, not in the tissues that are sutured together, but is due to an excoriation and ulceration of the skin of the perineum and sometimes the anus, from being in contact with the

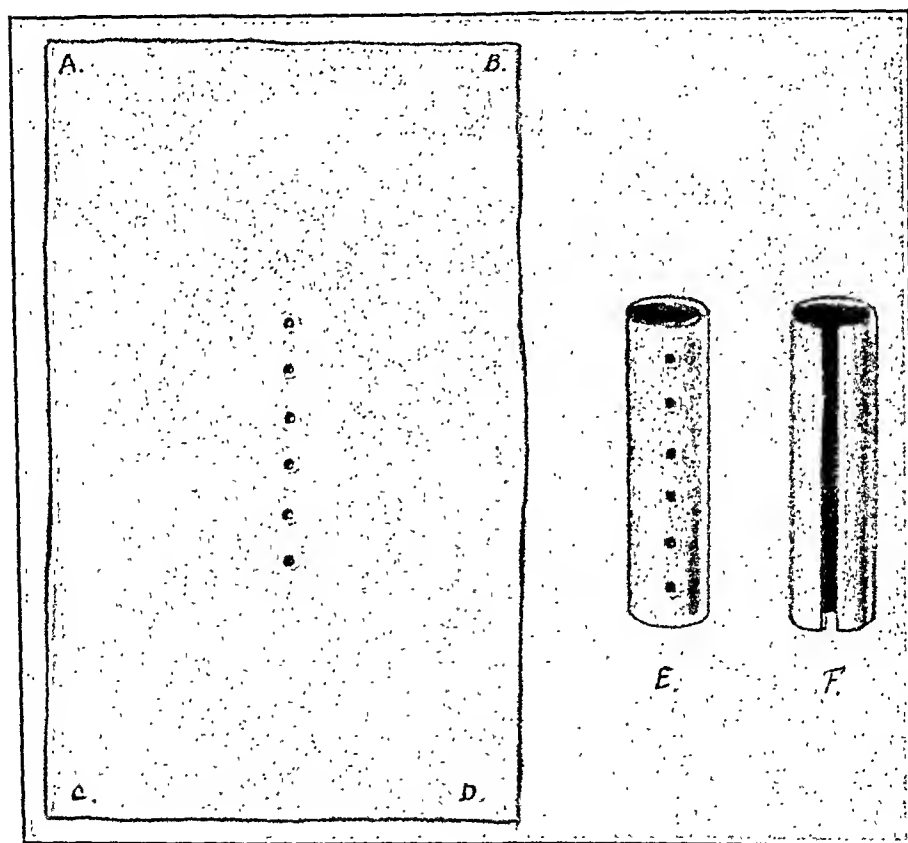


Fig. 1.

ends of the sutures. This discovery led me to devise a means for the elimination of the discomfort.

The procedure suggested has succeeded in eliminating pain in an astonishing manner.

The method consists in preparing two articles. The first is a piece of rubber tissue like that from which surgeons' gloves are made. The piece should be five inches long and three inches wide, as shown in Fig. 1. In the center of this rubber sheet six or seven tiny holes are burned with the point of a pin which has been brought to a red heat by spirit lamp or Bunsen burner. The second article is a piece of rubber tubing

\*Presented at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, April 23, 1935.



one-half inch in diameter and two inches long, capable of maintaining its round shape. On one side of the curve of the rubber tube six or seven tiny holes are

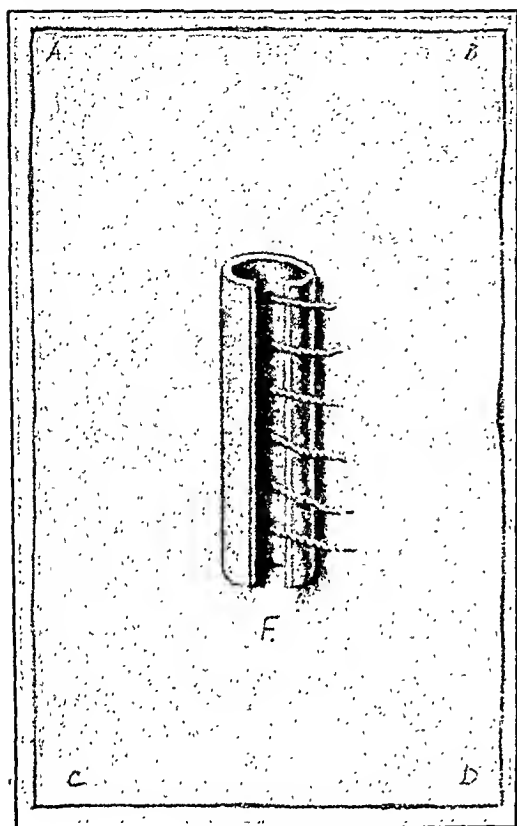


Fig. 2.

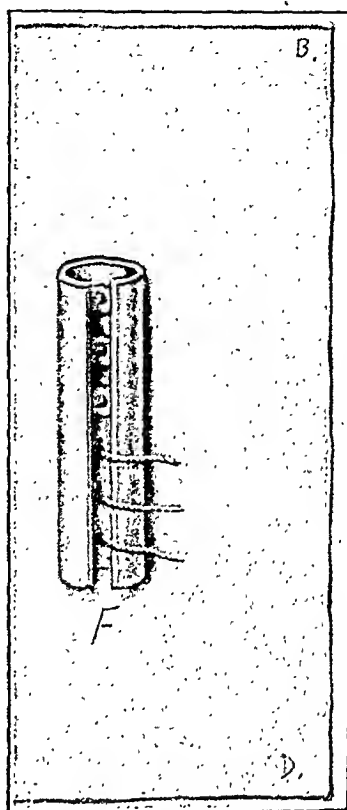


Fig. 3.

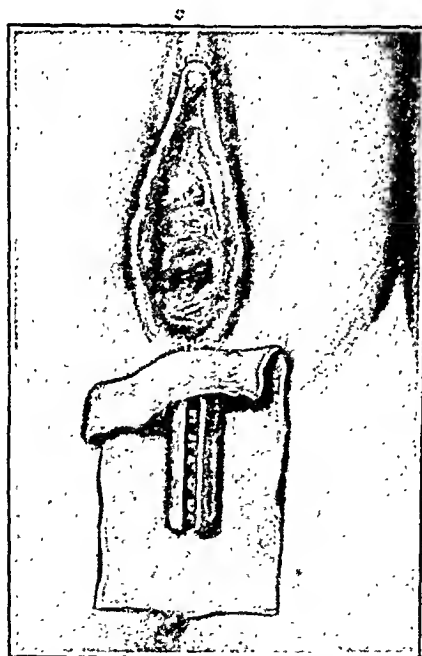


Fig. 4.

burned in a straight line with the hot point of a hat pin (Fig. 1, E). On either side of this tube opposite where the holes were made, the tube is split through its

entire length in a straight line, so that the tube can be opened up and when pressure is released the tube closes up again (Fig. 1, F).

After the ends of the silver wire have been twisted the rubber sheet is spread on the perineum and the ends of the silver wire are pulled through the small opening. The rubber tube is threaded on the silver wire (Fig. 2). The fine rubber sheet A.B.C.D. and rubber tube F. are now in place (Fig. 2). Over each wire is threaded a perforated lead shot, pushed down in the lumen of the tube and made to grasp the wire by flattening the shot. The superfluous portion of the wire is then cut off flush with the perforated shot (Fig. 3). The flattened shot holds the suture firmly and lies entirely within the lumen of the rubber tube. The ends of the suture and shot cannot rub against the patient's skin, as they are entirely hidden in the tube. The rubber sheet which has first been placed on the perineum, is now tied over the rubber tube with a piece of silk (Fig. 4). The last step is for the purpose of protecting the upper and lower ends of the rubber tube from causing excoriation, which will occur if it is not covered with the soft rubber sheet.

225 CENTRAL PARK WEST

## ANENCEPHALIC MONSTER COMPLICATED BY AN IMPACTED OVARIAN CYST

LOUIS RUDOLPH, M.S., M.D., F.A.C.S., CHICAGO, ILL.

(From the Obstetric Service of the Cook County Hospital)

THIS case is reported in order to emphasize the value of roentgenography in obstetric practice and of laparotomy for a surgical indication during the latter months of pregnancy with a normal or an abnormal fetus that does not call for the removal of the fetus by hysterotomy.

Mrs. B. J., aged eighteen years, white, primipara, married to a Filipino. The family and the personal history were of no importance. The last menstrual period Aug. 15, 1934. At term May 22, 1935. The patient was admitted to the Obstetrical Department of the Cook County Hospital on March 6, on account of a suspected dead fetus. Patient stated that she had not felt life for two weeks previous to admission.

*Physical Examination.*—A young white female in good general health. She had no abnormal subjective complaints. The uterus was of normal consistency and shape, but upon abdominal examination appeared to be at term. Fetal movements could not be palpated. Fetal heart tones absent. No placental souffle present.

*Vaginal Examination.*—The vagina was obstructed by a cystic mass which took origin in the posterior vaginal wall and extended into the fornices. The cervix was displaced upward behind the symphysis pubis, and the external os was at the level of the superior border of the symphysis pubis.

*Laboratory Examination.*—Kahn test negative. W.B.C. 7,650. Urine negative.

Roentgen examination made on March 7 showed an anencephalic monster in a transverse position and high in the abdomen.

*Diagnosis.*—Anencephalic monster complicated by an ovarian cyst.

*Treatment.*—Laparotomy for removal of the cyst without interrupting the pregnancy.

On March 15 a laparotomy was performed. The ovarian cyst could not be delivered into the field of operation. The cyst originated from the left ovary. The ovarian pedicle was brought forward as much as possible, which brought the cyst more anteriorly, a trocar was inserted into the cyst, and after the removal of

800 c.c. of a yellow fluid the ovarian cyst was delivered into the field of operation. The usual oophorectomy was performed. The uterus was not disturbed and the abdominal wound was closed in layers.

*Diagnosis.*—Cystadenoma serosum. The cyst was unilocular and was 13 cm. in diameter.

*Postoperative Course.*—From the second postoperative day the patient experienced irregular uterine contractions. On the seventh postoperative day these became stronger and in one hour she delivered herself of a macerated anencephalic monster spontaneously. The patient made an uneventful recovery and was discharged from the hospital on the ninth postpartum or the sixteenth postoperative day.

55 EAST WASHINGTON STREET

---

## CONTROL OF RESTLESSNESS IN PAINLESS LABOR

R. A. BARTHOLOMEW, M.D., AND E. D. COLVIN, ATLANTA, GA.

A SYMPTOM common to some patients under the effect of an amnesic agent or combination of agents during labor, is a tendency to restlessness during the pains and even between the pains. This symptom, while of no particular consequence during labor, may be quite troublesome during preparations for delivery and actual delivery, due to the difficulties of local cleansing of the patient, keeping the sterile drapings in place and holding the patient in position. This seems to be one of the objections most frequently raised by the physician who has not yet allowed himself to be converted to the use of amnesic agents during labor.

While this symptom has not been present to a troublesome degree in our experience of the past two years, with the use of paraldehyde and sodium amytal or pentobarbital sodium<sup>1</sup> in obtaining painless labor, we have been impressed with the desirability of some method of control of the restlessness manifested by certain patients, particularly just before and during delivery, and have found the following procedures most helpful and free from harm.

During the latter part of the first stage and throughout the second stage, while the patient is in the labor room, moderate restraint of the arms by the use of wrist cuffs fastened to the side of the bed to permit only a limited movement of the arms, to prevent self-contamination of the vulva, and to keep the patient more on her back, has been found to be of great aid. This restraint should not be applied until it is evident that the patient is thoroughly under the effect of the injection.

During the latter part of the second stage, ether, a mask, and a sterile towel are placed conveniently near the bed. Progress is allowed to continue until, in nulliparas the head remains visible between pains and the perineum begins to stretch, and in multiparas the perineum bulges well or the head is visible during pains. Counter pressure with the sterile towel may be used if progress increases too rapidly. Ether is then given with as little disturbance as possible, to the stage of very light primary anesthesia. Pains will be temporarily slowed and the patient thoroughly relaxed. She is then moved to the delivery room and lifted from her bed onto the delivery table.

Meanwhile the nurse has scrubbed and is ready to prepare the patient at once. A small amount of ether is continued and by the time the local preparation is completed, strong pains already have returned or may be stimulated with extract of pituitary. Episiotomy under local anesthesia may permit prompt birth or, if neces-

<sup>1</sup>J. A. M. A. 104: 362, 1935.

sary, the head may be lifted over the perineum with forceps. Spontaneous crowning and delivery is the rule.

The use of ether in this manner, effectively prevents any interference on the part of the patient, with the final preparations for delivery, facilitates control of the patient and does not cause increased bleeding during or after the third stage. The condition of the baby at birth is apparently not affected by this small additional dose of ether.

It is hoped that these suggestions may be helpful to those who have found an orderly obstetric technic handicapped by the restlessness which occasionally complicates amnesia during labor.

1040 PONCE DE LEON AVENUE, N. E.

---

Clauberg, C.: Studies on the Infantile and Deficient Human Uterus, *Ztschr. f. Gynak. & Geburtsh.* 107: 328, 1934.

Both the infantile and the secondary atrophied (through castration) uteri in the rabbit respond to the injection of follicular hormone. The degree of growth varies in these two groups since the secondary atrophied uterus responds faster to a smaller dose and with greater regularity. It is as if a uterus, once having been under hormonal influences, is in greater readiness to react anew to these stimuli. These observations made on the rabbit were duplicated in the human being. Intra-uterine lipoidol-injections, checked by x-ray pictures, measurements of the uterine cavity through the sound, and curettage were employed to register the effect of injections of larger doses (between a 150,000 and 300,000 M.U.) of progynon. One castrated woman received 160,000 M.U. over eight days; another, having been amenorrheic over thirteen years, received 200,000 M.U. over fifteen days. The uterine cavities in both cases increased their capacity enormously, as demonstrated by x-ray. Menstrual-like bleedings occurred six to nine days, respectively, after treatment but three months after termination of treatment the uteri were smaller again. The group of infantile uteri comprises seven patients; all had small uteri, were amenorrheic over long periods of time and had never been pregnant. The dosage used was close to 300,000 M.U. within approximately twenty-one days. Five of the seven flowed from six to ten days after the last injection. Two received over 300,000 M.U., but did not respond with a bleeding. The x-ray pictures of all seven showed an enlarged uterine cavity. Two women with normally developed and functioning uteri were given large doses of progynon; an increase in size of the uterus could be demonstrated.

In these investigations the observation was made that the cervical part of the uterus responds more to the follicular hormone than the body of the uterus. The cervix becomes hyperemic, soft and is more easily dilated. The flow in all cases was in no way different from menstruation. A possible harmful effect of such large doses was considered but could not be demonstrated.

GROVER LIESE.

# Department of Maternal Welfare

---

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

---

## THE AMERICAN COMMITTEE ON MATERNAL WELFARE\*

MEETING HELD AT ATLANTIC CITY, JUNE 12, 1935

### CHAIRMAN'S ADDRESS

FRED L. ADAIR, M.D., CHICAGO

THE American Committee on Maternal Welfare was originally formed as the Joint Committee on Maternal Welfare. The establishment of this committee was the result of a resolution passed in 1919 by the Association for the Study and Prevention of Infant Mortality. This resolution called for the cooperation of the American Gynecological Society and the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons. The Joint Committee was formed by three representatives from each of these organizations. Later a collaborative committee was formed from the American Pediatric Society. Subsequently the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association participated in this Joint Committee by appointing three members to represent it. Members of this Committee not only have participated in its work, which has resulted in the publication of certain standards on maternity care, but also have stimulated activity among various medical groups throughout the country by correspondence and the promotion of educational programs among medical organizations. It has also participated actively in an advisory capacity in the work of the Federal Children's Bureau; furthermore, most of the members were active in and spent a large amount of time in developing the work of the White House Conference on Child Health and Protection in 1930.

This Committee has had very meager financial support and has never been in a position to carry on its work in any way except through the volunteer efforts of its members, although small contributions have been received from some of the component societies.

Ultimately it was decided that the committee was of sufficient importance to be incorporated. This was accomplished on April 16, 1934, at which time the name was changed to American Committee on Maternal Welfare. The official purpose of this committee, as stated in its by-laws, is as follows:

"The object for which this corporation is formed is to awaken and stimulate the interest of members of the medical profession in cooperating with public and private agencies for the protection of the health of mothers and their offspring before and during pregnancy and labor, and after confinement, to the end that the conditions which menace and interfere with the health or life of the mother or infant may be improved or prevented, and disease and disorder corrected and prevented, health promoted and life saved; to teach the principles and practices of general and personal hygiene and health to parents; to improve and generalize the standards and methods of training physicians, nurses, and others dealing with problems of maternity; to study and promote the study of the problems involved in achieving the foregoing

---

\*For lack of space it is possible to publish only an abstract of these proceedings; a complete account may be found in reprints obtainable from the Chairman, Dr. F. L. Adair, University of Chicago, Chicago, Ill.

objects; to publish and circulate publications of any kind and description; to receive donations, and to purchase or acquire, receive, take, hold and manage such real and personal property by gift, grant, devise or bequest as may be necessary, useful or desirable for the purposes and objects of the corporation above set forth.''

Since incorporation, various organizations in addition to those previously enumerated have been invited to identify themselves officially with this Committee and to appoint a representative from their organization to represent it at the meeting, including now: The American Association of Obstetricians, Gynecologists, and Abdominal Surgeons; American Child Health Association; American College of Surgeons; American Gynecological Society; Section on Obstetrics and Gynecology of the American Medical Association; American Public Health Association; Central Association of Obstetricians and Gynecologists; Chicago Maternity Center; Children's Bureau, U. S. Department of Labor; Maternity Center Association of New York; Pacific Coast Society of Obstetrics and Gynecology; and the Southern Medical Association.

Since its incorporation the Committee has attempted to stimulate the formation of state committees on maternal welfare and their work is now in active progress. Some states already had committees functioning in this capacity, but most of them had not. One of two plans of procedure has been followed in the formation of these state committees. The first contemplated official action by the State Medical Societies in the formation of such a committee with the thought that each state committee would guide and direct the formation of local committees in each of the county or district societies of its state. This plan was preferred because it was felt that a maternal welfare program would in this way become an official part of the activities of the various state and local medical societies. In the states in which this plan does not appear to be feasible, the national committee has endeavored to secure the active interest of members of the medical profession in leading the activities in their state and in securing the appointment of the necessary local committees throughout that state. The national committee has felt that it should not in any way attempt to dictate the activities of these various committees. It does sincerely believe that such activities on the part of obstetricians and general practitioners are not only advisable but essential for the welfare of both the mother and her infant upon whom the future of the community rests.

Without entering into a discussion of comparative morbidity and mortality in mothers and infants, we are convinced that in most communities the rate for both can be reduced. We are also certain that this can be obtained only by the practice of safe and sane obstetrics during the antepartum, intrapartum, and postpartum phases of obstetric care. Optimum results cannot be accomplished in a day but will be achieved only through the long-continued efforts of those medical men who are sincerely interested in furthering improved maternity care. The practitioners of obstetrics cannot accomplish this unaided, as such efforts must be combined with a corresponding interest and endeavor on the part of the laity and particularly with the cooperation of nursing organizations. The results of cooperative effort among these interested groups would far exceed any results which could be obtained by individual effort. The securing of adequate maternity care, while it requires individual effort with reference to individual patients, must not be regarded any longer as a matter of solely individual concern. It is as much a matter of community interest as any other endeavor directed toward the lowering of morbidity and mortality rates.

Community efforts must be directed toward the development of their own resources for adequate and consecutive maternity and infant care. This implies the utilization of facilities for the proper care of patients in their homes, in offices and clinics, and in hospitals where adequate and special provision is made for the care of mothers and their newborn infants, both premature and mature. Such facilities can be

developed and utilized only by the combined efforts of obstetric practitioners, nurses, and others interested in the development of health activities which pertain to maternity and infant care.

One concrete suggestion which the American Committee on Maternal Welfare has made is that each state and local committee should study its own resources with a view to supplementing and developing them as need arises. It is to be hoped that recognition of the adequacy or inadequacy of these facilities will lead gradually to the development of more complete programs of maternity care for these communities.

Our Committee has already recognized the desirability of setting up certain standards for maternity care during the antepartum, intrapartum and postpartum phases, and, although it has published some of these standards, it is proposed that they be revised and elaborated for the benefit of those who desire to utilize them. Other standards, too, seem to be requisite. A lack of them both in this country and abroad has led to more or less confusion in understanding the results already obtained. Mortality is one of the simplest of problems to study statistically, and yet studies of maternal mortality have been very difficult to evaluate, especially for comparative purposes and from the viewpoint of determining the value of varying procedures. Analysis of data relative to morbidity is even more confusing because there are no generally accepted standards of fetal, infant, or maternal morbidity. Morbidity has, as a rule, been studied merely from the standpoint of incidence of a certain temperature rise, but there has been no general agreement as to what degree of fever should be accepted. Inasmuch as such studies have comparative value only, it seemed wise for the Committee to advocate the adoption of a definition of febrile morbidity. The Committee has, accordingly, defined febrile maternal morbidity to be a fever of 100.4° F. (38° C.) or over on any two of the first ten days postpartum, exclusive of the first twenty-four hours; the temperature should be taken by mouth by the standard technic at least four times daily.

This, however, is only one of a number of standards which should be adopted. If one attempts to define puerperal infection or puerperal septicemia, difficulties immediately arise, because such a condition does not constitute a well-defined entity. Certain states have required the reporting of puerperal septicemia, but their attempt has been more or less of a fiasco and has led to no definite results. So far as the fetus is concerned, there is no clear-cut definition as to what really constitutes a stillbirth and what a living birth. There is no general agreement as to what fetal size, weight, or period of gestation constitutes viability. There is no clear-cut definition of a premature infant, and, so far as fetal and infant morbidity are concerned, there are no definable conditions which can be studied comparatively in different institutions. It is important to recognize other factors of morbidity than fever. Hemorrhage causes morbidity. Trauma is productive of morbidity. And yet we have no definite standards for defining clearly either these or the many other morbid conditions.

Our Committee necessarily is vitally interested in obstetric education, not only of the laity, but also of those groups which concern themselves especially with maternity care. Among these groups may be mentioned social service workers, nurses, in addition to physicians. We should be interested in furthering improved standards of education for these groups. It is not my purpose to discuss education in relation to the activities of these various personnel groups, but it should be emphasized that theoretical knowledge, however good, is not sufficient and that actual experience is essential to the carrying on of the best work in this as well as in other fields of endeavor. So far as medical practice is concerned, and with particular reference to

obstetric practice, only eighteen states and eighteen medical schools of the United States and Canada require an internship as a prerequisite to the practice of medicine and the granting of an M.D. degree. These are:

MEDICAL SCHOOLS	STATES
University of California	Pennsylvania
College of Medical Evangelists	New Jersey
University of Southern California	Rhode Island
Stanford University	North Dakota
Loyola University	Washington
Northwestern University	Michigan
University of Chicago,	Wyoming
Rush Medical College	West Virginia
University of Chicago,	Oregon
Division of Biological Sciences	Illinois
University of Illinois	Delaware
Louisiana State University	Iowa
Wayne University, formerly Detroit	South Dakota
College of Physicians and Surgeons	Utah
University of Minnesota	Wisconsin
Duke University	District of Columbia
University of Cincinnati	Oklahoma
Marquette University	Vermont
Canada:	
University of Manitoba	
Dalhousie University	
University of Montreal	

Practically none of these schools or states requires that experience in obstetrics be an essential part of the internship.

It would seem that one very important function of our Committee could be an attempt to secure such requirements and regulations as would make it essential for those engaging in obstetric practice to obtain at least a minimum of training in these fields.

It is important to realize that the families of this country are vitally interested in improved maternity care. The doctors must realize this desire and attempt to satisfy it. It is needless to call your attention to the legislation already enacted and in process of enactment which comes as an answer to this call for better conditions to surround maternity and early infancy. The physicians of this country can and must be in a position, not only to hear this call, but to answer it satisfactorily.

We have attempted to prepare a short program which will give you in brief detail some idea of a few of the activities contemplated in various sections of the United States. The following papers were presented:

"The Cleveland Plan." By A. J. Skeel, M.D., Cleveland, Ohio.

"Organized Maternal Welfare Work in New Jersey." By Arthur W. Bingham, M.D., F.A.C.S., East Orange, N. J.

"Maternal Welfare Work in New York." By J. T. Quigley, M.D., Rochester, N. Y.

"The Plan of Action, Aims and Progress of the Pennsylvania Commission on Maternal Welfare." By James S. Taylor, M.D., Altoona, Pa.



# Society Transactions

## AMERICAN GYNECOLOGICAL SOCIETY

### SIXTIETH ANNUAL MEETING

*Hot Springs, Va., May 27, 28, 29, 1935*

*(Continued from the November issue)*

#### DISCUSSION

**1. Further Studies on the Mechanism of Labor.** Drs. William E. Caldwell, H. C. Moloy, and D. Anthony D'Esopo, New York City. (For original article, see page 763.)

DR. WILLIAM E. STUDDIFORD, NEW YORK CITY.—We have at Bellevue Hospital a precision stereoscope and I consider that this method of study of the pelvis and of the patient in labor has been of enormous assistance to us. A great many cases which have puzzled us, after study with this procedure, have been clarified. The method also has been of marked help in teaching the interne staff and medical students what actually goes on during labor.

DR. F. G. GOLDSBOROUGH, BUFFALO, N. Y.—It seems to me that this work is particularly useful at the present time when the tendency in obstetrics is so much toward operative procedures which are giving rather poor results. Where the greatest number of operative deliveries are being done the maternal mortality is high. The more these cases are studied the better will we be able to predict whether trouble will occur, and to know beforehand whether we shall be able to get a satisfactory result by delivering through the pelvis rather than by cesarean section.

**8. The Place of Colpectomy in the Treatment of Uterine and Vaginal Prolapse.** Dr. Louis E. Phaneuf, Boston, Mass. (By invitation.) (For original paper, see page 544, October issue.)

#### DISCUSSION

DR. W. T. DANNREUTHER, NEW YORK, N. Y.—Dr. Phaneuf has used the term prolapse in its broadest sense, to include descent through the vagina of any or all of the pelvic structures. From the practical standpoint, it is desirable to subdivide patients with such lesions into three groups: first, those who are candidates for surgical repair for the first time; second, those in whom ineffectual or inadequate attempts at operative correction have already been made; and third, those who suffer from complete inversion of the vagina after abdominal or vaginal hysterectomy.

In the first group, the experienced pelvic surgeon has a wide choice of available technical procedures and will select those which are best adapted to a particular case. His choice will depend upon the patient's age, marital state, the likelihood of future pregnancy, the extent of damage to the vaginal structures, and the coexistence of either uterine or adnexal pathologic conditions. Only in elderly patients and under exceptional circumstances will any form of vaginal closure be justified in this group of patients. I have done a LeFort colpocleisis under local anesthesia in three widows over seventy years of age with great satisfaction. On the other hand, I

made the mistake of doing the same operation in an obese virgin of fifty-six with a complete procidentia, and was soon thereafter confronted with extensive recurrence.

In the second group, the operator will often be compelled to exercise his surgical ingenuity, not only to correct the prolapse, but to undo what has unwisely or improperly been done previously. The Jackson operation has served me in good stead in several such instances. Some patients are compelled to return because of the neglect of an enterocele or posterior vaginal hernia at the time of the original operation. When the uterus is still in situ, and a colpoeleisis is performed, the subtotal operation is preferable to a complete colpectomy, because it makes provision for drainage, and even normal mucus can always escape.

The third group is the one in which complete colpectomy is most frequently indicated, and in which colpoeleisis, both partial and complete, may most often be utilized without regard for anything other than the cure of the everted vagina. Nearly all of these patients are advanced in years and are not concerned with vaginal patency. Occasionally, however, a relatively young woman will require some other solution of her problem. In one such instance I opened the abdomen, dissected the bladder free, and reconstructed a firm pelvic support by building a platform under the bladder, consisting of the laterally overlapped broad and round ligament stumps, and the split apex of the vaginal tube. This cured the inversion. In another case I fixed the apex of the elongated vagina to the abdominal wall, but neglected to split the top and denude it of mucosa, as advocated by Crile. This operation eventuated in recurrence, and the patient was subsequently cured by a LeFort operation. Norman F. Miller has suggested opening the anterior vaginal wall, doing a Rawls cystocele operation, and pulling the prolapsed vagina up by "lifting" sutures inserted at the base of the uterosacral ligaments. Miller reports two successful cases.

The great advantages of colpoeleisis and colpectomy are the simplicity of technique, the dispatch with which they can be done under local anesthesia, and their freedom from hazards even in poor surgical risks. In doing the LeFort operation, I have found it of advantage to place one Pagenstecher linen suture at each corner of the rectangular denudation. Like Dr. Phaneuf, I have done a vaginal colpoeleisis about 25 times without any morbidity or mortality.

DR. FREDERICK C. HOLDEN, NEW YORK CITY.—I am convinced that the LeFort operation has a definite field of usefulness, and have performed this operation 31 times within the past eight years. Prior to 1927 I performed complete colpectomy in two cases, making a total of 33 cases.

In 1929, Baer reported to this Society a series of 220 patients operated upon for prolapse; in 14 of these the LeFort operation was done. In discussing Baer's paper, Gellhorn correctly said that the LeFort operation had fallen into an entirely undeserved oblivion. Very few books describe this operation. In Davis' *System* and in Curtis' *Obstetrics and Gynecology* there is no mention made of it. I had never seen the operation performed until after I did my first case in 1927. I believe the reasons why this very satisfactory operation, which was described in 1877, went into the discard were: first, that at that time the only suture materials available were silver wire and silk; second, the high muscle perineal repair was unknown; third, the cases may not have had adequate preoperative preparation.

I note that Dr. Phaneuf amputated the cervix in five cases. In none of my cases have I had occasion to amputate a cervix. Many had extensive ulceration of the cervix caused by the trauma of being sat on, but in all such cases a period of preoperative treatment completely healed the cervical lesions.

One patient entered the hospital with a complete irreducible prolapse which was reduced only after the patient had been in a very high elevated foot posture with continuous applications of warm wet dressings for forty-eight hours. She required local treatment for about two months, due to the extensive ulceration and brawny induration of the vaginal and cervical lesions, but she made a splendid recovery.

Before that time I had seen three complete irreducible prolapses which remained unreduced despite treatment and all of these patients died of sepsis.

In my series of 31 cases, the age varied from 50 to 77, the average being 62. The anesthetics used were morphine and scopolamine, local or spinal, and gas oxygen.

I had one fatality. The woman, sixty years of age, was referred from the medical service to which she had been admitted with marked ecchymosis of both arms and legs. She was mentally clouded and unable to state exactly why she came to the hospital. She had had very little to eat in the past few months. The discoloration on the extremities cleared up promptly under an antiscorbutic diet. The anesthesia used here was a small dose of novocaine intraspinally. She died on the fifth day postoperative from bronchopneumonia. The results in the other 31 cases were excellent. For cure of the prolapse in those who have passed the age of sex life, even though the general condition may be poor, the LeFort operation can be done with comparative safety, and with uniformly excellent results.

DR. CAREY CULBERTSON, CHICAGO, ILL.—I have performed colpectomies in three women, 63, 69, and 69 years of age, where the extruded vaginas, twelve, fifteen, and twenty years after previous hysterectomies, were so badly diseased as to render any simpler procedure impossible. In these cases ethylene gas or nitrous oxide gas were the anesthetics.

Hystero-colpectomy was carried out in six patients, 62 to 76 years old with the exception of one who was 54. In all of these the entire vagina was taken out because of disease on its own part, the uterus coming out incidentally. Scopolamine-morphine with novocaine infiltration was the anesthetic in all except two, where ether was used.

In five other patients who were younger, extrusion of the vagina had occurred, in two after subtotal abdominal hysterectomies, and in three after total hysterectomies. In all of these it was necessary to preserve the lower genital tract, the patients varying in age from 36 to 49 years. The two who had a cervix were repaired by the old operation of fixation of the stump into the abdominal wall, abdominal trachelopexy. The other three women were treated by what may be called vagino-abdominal ligamentopexy; that is, opening of the vaginal vault and, by abdominal incision, fixing it with such ligamentary structures as could be found or made. These operations were all associated with perineorrhaphies of course, and were technically successful. Ether was the anesthetic in two of these, ethylene gas in two and nitrous oxide in one.

The safest and simplest of these various procedures for elderly women is the operation proposed years ago by Neugebauer and then by LeFort. I have employed this anteroposterior colpocleisis in seventeen patients, all with fortunate results. I prefer to limit the operation to women in the sixties and seventies who will no longer work hard. One of my patients was only fifty-seven years of age, a widow suffering from severe myocarditis, until she was unable to walk upstairs. The LeFort operation was done under scopolamine-morphine anesthesia eight times, with ethylene gas four times, and nitrous oxide three times. In one case ether was used, it being the only anesthetic available. The results have been uniformly good and there has been no recurrence.

In a certain number of cases the cervix does not yield readily to preoperative treatment or is only superficially eroded. In eleven of these seventeen cases I

trimmed it off squarely and rolled it in with the closure. These elderly women do not have a cervical or uterine discharge, in some cases they do not have a cervical canal, and I do not hesitate, for that reason, to amputate the cervix superficially in the denudation.

Dr. Holden has emphasized the point of building in a perineum below. The anterior vaginal wall is nearly always shorter than the posterior, and if the fourchet denudation is flared out laterally and obliquely, then approximation from side to side, after the colpoeclisis is effected, constitutes a perineorrhaphy.

DR. GEORGE GELLHORN, ST. LOUIS, MO.—In the elderly women in whom this operation is performed, any general anesthesia is, as a rule, contraindicated. Spinal anesthesia is too dangerous; it is like shooting at little birds with a big cannon. All that is needed here is local anesthesia, and less than two ounces of a one-fourth per cent novocaine solution with adrenalin are sufficient to produce a complete analgesia.

Dr. Dannreuther's failure with this operation cannot be laid at the door of the LeFort technic. I had a very similar case of total prolapse in a girl of fifteen years in whom the condition had existed for seven years. In this instance, as well as probably in Dr. Dannreuther's case, we have to bear in mind a constitutional anomaly which manifests itself in an abnormally deep and wide culdesac. The best method of procedure in such a case is an abdominal operation, complete obliteration of the culdesac by suture, and the production of an incline that leads obliquely down from the promontory to the symphysis so that the small intestines cannot enter and produce what eventually amounts to an enterocele.

DR. GEORGE GRAY WARD, NEW YORK, N. Y.—Two weeks ago I saw a woman in her thirties who had a congenital absence of the vagina. Some one had done a Baldwin operation on her and she has an artificial vagina which is excellent so far as the depth and function are concerned. This patient had developed an abscess of the perineum which resulted in destruction of the sphincter ani, so that there was no perineal body and now when she strains, this artificial vagina comes out and hangs outside the body, like a glove finger. I would like to ask Dr. Phaneuf if he has any suggestions how to handle this case.

MR. VICTOR BONNEY, LONDON, ENGLAND.—I have done LeFort's operation for a great many years on elderly women, and it is admirable in that class of case. I would suggest that instead of suturing the two halves of the vagina directly together so that the line of union has no depth or thickness, it is well to invert the edges so as to get a greatly increased area of adhesion. The septum is much stronger and broader when sutured in this way. I usually employ mattress sutures passed through the flaps so that the loops lie on the vaginal surface. The free ends of the sutures passed through the right-hand anterior flap are tied to the free ends of the sutures passed through the right-hand posterior flap, and similarly with the left-hand flaps. Alternatively two continuous sutures may be used, one on each side, each one passed with its loop on the vaginal surface like Connell's intestinal suture. The interrupted sutures, however, give the strongest result.

DR. FRED L. ADAIR, CHICAGO, ILL.—We have had 35 or 40 partial colpectomies, not any total colpectomies; death occurred in two cases. I do not know how you will avoid a casualty when operating on women at the age at which this is usually done. In patients with diseased cervices we have performed a hysterectomy in connection with the partial colpoeclisis. As Holden suggested, we tie the knots inside of the new canal, getting a fairly wide bite of the vaginal tissue in order to unite the walls. We frequently combine a cystocele operation as well as a perineorrhaphy and usually, instead of making a complete rectangular flap, we carry it down grad-

usually under the external meatus so as to tighten up the slack in the lower portion of the urethra. The point is that instead of removing the flaps in toto, we remove the flaps and suture as we proceed in order to minimize the blood loss.

DR. JOSEPH L. BAER, CHICAGO, ILL.—Since 1929 our staff has done 21 additional such operations which were reported last fall before the Central Association in New Orleans. Of the 21 operations, 20 were of the LeFort type, and 1 was a total colectomy.

In connection with the technic, it is our practice to approximate the raw surfaces by transverse sutures as well as the inversion sutures on each side which close the vagina and make the horseshoe-shaped drainage tract. In other words, we bring the raw surfaces together with very fine catgut as we turn them in layer by layer to insure hemostasis.

DR. PHANEUF (Closing).—Although in Boston ether is the anesthesia of choice, from year to year I have increased the employment of local anesthesia.

**9. Toxemia of Pregnancy, Dr. James R. Goodall, Montreal, Canada.**  
(For original article, see page 577, October issue.)

#### DISCUSSION

DR. WILLIAM J. DIECKMANN, CHICAGO, ILL.—Dr. Goodall's work would seem to indicate that the pathologic changes in the placenta are the cause of the toxemias of pregnancy. While we believe that the placenta is intimately associated with the toxemias, we do not believe that the lesions found in the placenta are the cause of the toxemia. If these pathologic changes in the placenta are the cause of the toxemia, then they should always be present in toxemia. Again, the placenta quite often may show marked pathology and yet the pregnancy has been normal. I would like to ask Dr. Goodall how to reconcile these conditions.

DeSnoo pointed out a number of years ago that many of the toxemias were characterized only by an increase in blood pressure. We have a sufficient number of cases now to make us absolutely certain that many of the cases of toxemia are primarily vascular diseases. We have not been able to decide in the majority of cases whether the patient had a predisposition to vascular disease which was aggravated by the pregnancy or whether the pregnancy per se has been the cause of the hypertension.

Dr. Goodall stated that changes in the blood chemistry are the result and not the cause of the toxemia and are of very little help in the differentiation of those cases which will have permanent vascular renal damage. We cannot agree with these statements in toto. We believe that the chemical changes occur early in the disease and, in fact, are a part of it. We have also been able to make use of these changes as a prognostic guide and in classifying the various types of toxemia.

The essayist stated that more attention should be devoted to the baby. In the toxemias of pregnancy the fetal mortality, both before and after delivery, is appallingly high, and we are becoming more and more pessimistic in our views as to the advisability of carrying toxemic patients for weeks in an endeavor to get a viable baby.

We have noted a marked incidence of abruptio placentae in patients with vascular disease. It may be that the changes in the vessels of the uterine wall, such as Dr. Goodall pointed out a number of years ago, are the cause of the premature separation of the placenta. We have also noted that the placental infarctions which were shown so beautifully are almost always present if there has been a marked albuminuria over a period of several weeks.

DR. FRED L. ADAIR, CHICAGO, ILL.—Some years ago we made extensive studies of the placenta, particularly with reference to Young's ideas in connection with eclampsia, and it seemed to me that we must have three postulates satisfied before we could accept this etiology. The first is that the lesions should be constant, second, that these lesions should not be present in normal placentas, and third, that they should not be present in other pathologic conditions of the mother which are not apparently related to the toxemias. In a series of cases which we studied, which represented a great many observations, we were unable to satisfy any one of these three postulates. We frequently found normal placentas, as far as we could demonstrate at that time, also we found lesions which appeared to be identical in patients who appeared to be normal, and lastly, we found similar or identical lesions in association with other conditions which were not related to the toxemia. We concluded that placental pathology was not the cause of the toxemia but was rather the result of these conditions that were associated with the toxemias.

We also carried on the study of the placenta in another series of cases in which we observed particularly the weight and surface area of the placenta in relation to the size of the child. We noted some of the pathologic changes that occurred in the placenta. One of our conclusions derived from the study was, though not quite so accurate as Dr. Goodall's, that less than half of the placenta is necessary to the survival of the child. Dr. Goodall pictures it more accurately at 25 per cent.

On the basis of our observations and those of others we feel that what has been called placental insufficiency is quite an important factor in the development of the fetus. If the placenta is sufficient up to a certain point, the fetus has a tendency to grow and may outgrow the placenta, and as the outgrowth occurs the child will die in utero. Other children do not die but do not grow to the extent of the normal child with a normal placenta, and we have been induced to name those infants immature. We have observed a number of infants who have the same relative size as the premature infant; they are much more vigorous but have not grown as they should have grown for their period of gestation. These results are related, we believe, to the physiology of the placenta and owing to the improper nutrition from the placenta do not grow, but their central nervous systems and their vital functions do mature and they are more apt to survive than premature infants of similar size, but less mature from the standpoint of gestation.

DR. COLLIN FOULKROD, PHILADELPHIA, PA.—I am sure that Dr. Goodall did not intend to convey the idea that, because of these lesions in the placenta, the cause of the toxemia was either fetal or placental in origin. In the latter half of pregnancy it is believed there exists a form of toxemia entirely related to pregnancy and that toxemia has important protean manifestations in the body and in the placenta. As we look at the diseases of the placenta, Dr. Goodall has shown us specimens containing nephritic changes which follow late in the course of the toxemia. Some of these hemorrhagic conditions are found in true nephritis, therefore there exists before those hemorrhagic conditions occur a condition of toxemia without nephritis, but the nephritis following may lead to hemorrhagic conditions. In the average patient the toxemia which follows nephritis may arise in the early part of the pregnancy. His point is rather well worth considering, that the toxemia is in itself an entity, finally showing itself in the death of the child.

I was surprised yesterday in the discussion of the hypothyroid patients that no mention was made of the fact that those of us who do not live in the goiter belt often see hypothyroidism in pregnancy and that it often leads to a form of toxemia, or is in itself a disturbance of metabolism that leads to the death of the child from perhaps a primary cause.

Hypothyroidism as we study it in our sterility clinics is divided into two classes: first, primary thyroid in origin, and second, the cases which if a careful evaluation of the pituitary is carried out will be found to be primarily pituitary, showing some deficiency of the thyroid, and the pregnant woman must have some of that pituitary impetus throughout the pregnancy to carry her to term. If we fail to furnish that impetus, there will be a dead baby and a disturbed condition in the body which usually in the hypothyroids involves all parts of the body. One might go over all of these protean manifestations and yet come back to the manifestations shown by Dr. Goodall, that there is one origin of these conditions. A study of such placentas must be viewed according to whether these patients were in the latter stages of toxemia or the period showing nephritic changes added to the toxemic changes.

DR. GOODALL (Closing).—It was most remote from my thought to convey the impression that the placental changes were the cause of toxemia. On the contrary, as Dr. Foulkrod has brought out, my contention is that it is the result of the toxemia and not the cause.

Dr. Adair's statement, which must receive consideration of course, is that in so many cases of toxemia we do not find any placental changes. That is just what I would expect. The law of susceptibility, of selectivity, comes in here with the utmost force and the placenta is susceptible more than any other tissue of the body possibly because it has a short life. It is a mushroom growth and most imperfect and it begins to undergo senile change at the seventh month. It is a very rare thing, extremely rare, to find a normal placenta at full term. That very senility predisposes to toxic changes and that is why the placenta, I think, is so frequently the selected point for the manifestation of the deleterious changes of toxemia.

A short time ago I outlined the various clinical types of toxemia depending for their variety upon the systems that are affected. We have the renal type in which the kidney is the one system with its vascular changes which bears the brunt of the attack. In others the kidneys do not seem to be affected at all and we have the vascular changes in which the blood vessels lose that power of discrimination whereby they allow certain things to pass through and certain ones not to pass through. In other cases we have no signs but in the nervous system, certain cataclysmic changes. And there is the other type where the liver seems to be affected chiefly. The selectivity, whatever the cause may be, I outlined in my paper last year in reporting five cases of nephritis "cured" by pregnancy. Now those are not nephritics; those are nephrotics. We cannot assume that their nephritis is cured by pregnancy, nor can we assume that those cases of the renal type are nephritic because the cessation of the pregnancy usually clears up the nephritis or the nephrosis in a few hours or a few days.

What I want to impress is that the placental changes are secondary and because they are not always found is no argument against the connection.

I agree with Dr. Studdiford that the hemorrhages are difficult to explain, but they are primarily thrombotic, due to changes in the blood vessels. I have demonstrated that to my own satisfaction repeatedly.

**10. Prophylaxis in Gynecology with Special Reference to the Immediate Care of the Postpartum Cervix.** Dr. Byron H. Goff, New York, N. Y. (Published in the current volume of Transactions.)

**3. The Treatment of Carcinoma of the Cervix by Wertheim's Operation,** Mr. Victor Bonney, London, England. (By invitation.) (For original article, see page 815.)

## DISCUSSION

DR. FREDERICK J. TAUSSIG, St. Louis, Mo.—In 1912, at the Baltimore meeting of our Society, I presented, in connection with a symposium, 60 cases done in the Midwest by the Wertheim operation for the treatment of cancer; 23 of those cases were done by me, and I had to acknowledge that my operative mortality in that series was 39 per cent. That was due to the fact that we had no other therapeutic resources; radium was not used at that time and in many cases operation was done in desperation where it should not have been attempted. Since that time, I have done, including those 23 cases, 87 Wertheim operations and the total mortality is 15 per cent. If we exclude this earlier group, and include only those operations done after 1912, my operative mortality has been reduced to 6 per cent. Eliminating also the cases that have been done since 1930 we find 43 cases done between 1912 and 1930 with two operative deaths, 4.6 per cent; and 26 cures for five years or more, 60 per cent. Of this number there were 23 patients who were operated upon over ten years ago, with one operative death and 10 living and well at the present time, 43 per cent ten-year cures.

This figure is due, of course, to the fact that I have as the result of my early experience been limiting the operation to Group I cases and no longer have included the Group II or borderline cases.

I do not agree with Mr. Bonney, however, in excluding the lost cases from calculation. All such cases have been classified in my series as recurrent. Nor can I entirely agree with his criticism of preoperative radiation. Wertheim used a cautery to clean up the cervix. It seems to me that radium is a very good method of cleaning up the cervix before operation and if the operation is done four or six weeks later we have an operative field that is clean, and there is less danger of implant metastasis. This, however, is not of much advantage where the lesion is less than 3 cm. in diameter.

The operability rate will vary with the institution. The lowest rate will be in a cancer hospital and the highest in university clinics and private institutions. I do not feel, therefore, that the operability rate has a great deal of significance. What is significant is the checking of our cases into groups, and we must be as honest as possible about this checking. If we adopt the League of Nations classification, comparisons can be more justly made.

The most interesting part of Mr. Bonney's paper is the report of the glandular involvement which I think was surprisingly high. In my own series where only Group II and a certain number of Group III cases were considered, the gland involvement was found to be 45 per cent. I am sure that in my Group I cases it would have been very much lower. It proves, however, very conclusively the necessity of considering metastasis in the gland in our treatment. Radiation effects upon cancer metastasis in the gland certainly have not been reliable. We have of course a certain number of sensitive tumors but in general no matter what may be the primary site of the cancer, the gland metastasis is better handled by surgery than by radiation, and I do not believe that the cervix cases are an exception in that respect.

I notice that when the glands were involved, Mr. Bonney's mortality was 20 per cent and there were only 22 per cent of five-year cures. That brings up the question whether we are justified in doing a radical Wertheim operation in the more extensive cases. If we do the glandular operation alone and treat the cervix by radiation, I think we will greatly reduce our primary mortality.

Since last year's report I have done 11 more operations of iliac lymphadenectomy for cervix cancer (a total of 39 cases in all) and have had but one operative death. I believe this operation therefore to be a safe procedure and one that is justified in the Group II cases.



In general my feeling as to the treatment of cervical cancer would be as follows: First of all, determine whether the case is a good operative risk. If there is obesity, if there is marked debility or extreme old age, if there are physical conditions such as a heart lesion or a kidney lesion or an endocrine condition that would make operation a material risk to that patient, then regardless of the involvement of the cancer I would not operate. However, let us consider what we would do if the case is a favorable one for operation: if it were a Group I case I would do a Wertheim operation with gland dissection since where it is limited to those earlier cases it is not so serious an operation. If we exclude the complicated cases we should get through with the Wertheim operation, have time to remove the iliac glands, and not lose more than 6 per cent of our patients.

In Group II cases I would on the basis of my experience thus far recommend the operation of iliac lymph gland removal with irradiation of the cervix. In Group III and IV cases I would recommend irradiation treatment alone.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—Unfortunately, in complimenting our guest on his technic, and in emphasizing the many operations he has so successfully performed, it is an inevitable corollary that we admit having reached approximately the maximum percentage of cures attainable by surgical means alone. Bonney's 33 per cent represents the greatest number of permanent cures obtainable by operative intervention.

I do not wish to discourage those who are advocates of radical surgery in the treatment of cancer of the cervix; their good work should go on. But statistics indicate that radium achieves an equal number of cures, with much lower morbidity and mortality. And we must remember that radiation therapy is still in its infancy, and the results are more and more satisfactory as our experience grows.

Stage I cases require no discussion; most of them may be cured either by operation or by radium. In patients with more widespread disease I have been greatly encouraged by the results obtained in my small series of cases with coincident surgical exposure and radium therapy, aided, as all cervical cancer cases should be, by intensive x-ray treatment.

DR. BENJAMIN P. WATSON, NEW YORK, N. Y.—Mr. Bonney has given us just such a presentation of his subject as we would expect from our knowledge of his writings and of his personality—clear, unequivocal, direct, and logical. Any man who has performed a particular operation 485 times has a basis from which to draw conclusions. He is to be congratulated on the reduction of his operative mortality from a high of 20 per cent in his early cases to 9.5 per cent in his more recent ones. I wonder if this mortality could not have been reduced further if more of the patients had had preliminary radiation to clear up the ragged, breaking-down carcinomatous tissue so often present.

I believe that in the present state of our knowledge regarding the behavior of the cancer cell, we are not in a position to be dogmatic about the treatment of cancer of the cervix. We all have seen cases in which radiation has absolutely failed to stay the course of the disease. We all have seen cases in which the radical operation in what appeared to be a very early case has been followed by death from cancer within a year or eighteen months. Our hope for the future must lie in the possibility of being more certain than we are now as to which type of cancer cell is radiosensitive and which radioresistant; which is more likely to metastasize early, and which late. Only then shall we be in a position to recommend with confidence radiation or operation or a combination of the two. The cancer cells are not all of the same type in the same case; the part removed by biopsy may differ materially from the rest of the lesion. Theoretically it would seem therefore that in the pres-

ent state of our knowledge the combination of radiation and operation in the so-called operable cases is the ideal when an operator with the skill of Mr. Bonney is available.

When such is not the case there can be no doubt that radiation alone will give the better ultimate results—with this proviso, that as it is unjustifiable for the inexperienced operator to attempt a Wertheim operation, so is it unjustifiable for the individual with no real knowledge of the technic of radiotherapy to treat the casual case.

DR. GEORGE GRAY WARD, NEW YORK, N. Y.—Bonney's work and large experience and the results he has obtained with the surgical treatment of carcinoma of the cervix represent the utmost we may hope to accomplish by pure surgery in this disease.

While his primary mortality in 483 cases is 14 per cent, in the last 200 cases he has reduced it to 9.5 per cent as a result of his experience and improved technic. When we consider that he has operated upon all cases whenever he thought there was any chance of completing the operation, his low primary mortality as compared with that of the average is remarkable and is proof of his great ability.

It is also remarkable that all his successful cases have not had the possible benefit of high voltage x-ray therapy, yet his survival rate approximates the best obtainable in any clinic whether surgery or radiation therapy has been employed.

I am glad that he gives us his ten-year results as well as the five-year, as we feel strongly that the ten-year period is of much greater value in estimating the actual cure rate. I am not quite so sure that we can agree with his statement that the ten-year period is a 100 per cent cure.

My records show one patient who survived eleven years and ten months and died after one year of symptoms from generalized carcinoma; another survived eleven years and two months and died of carcinoma of the pylorus; still another lived ten years less two months and died of the same condition.

His absolute five-year cure rate based on his assumed operability rate of 63 per cent is 24.6 per cent, and his relative rate is 25.6 per cent. This closely approximates the cure rate usually obtained by pure irradiation therapy in clinics here and abroad.

Our own five-year rate at the Woman's Hospital in 457 cases is 24.29 per cent absolute and 25.28 per cent relative.

Our ten-year cure rate of 17.79 per cent absolute and 18.31 per cent relative also approaches Mr. Bonney's ten-year figure of 18 per cent absolute and 20 per cent relative. Our figures here given were also obtained without the benefit of high voltage x-ray therapy. Our radium operability is 96.1 per cent.

As Mr. Bonney operated upon many well-advanced cases, it may be open to question whether the radiologist treating his 37 per cent inoperables can achieve a 12 per cent salvage in this group, which would give him a theoretical salvage of 30.6 per cent five-year cures.

The value of palliation by radium therapy should not be forgotten. The question of palliation should also be considered in the 14 per cent who died from the operation as compared to the 1 to 2 per cent primary mortality of radium therapy, as nearly all of this group would have survived radium treatment for varying periods.

Mr. Bonney gives his figures in two ways, uncorrected and corrected, the corrected figures by deducting those lost in the follow-up and those dead of other diseases. If we do likewise we naturally would improve our figures as we know of some 12 of our patients who apparently died of other causes. However, unless these cases were

autopsied, it is guesswork in many instances, therefore, the rule to class all cases lost track of or dead, as dead of cancer is probably more nearly accurate in the long run in estimating the value of the treatment.

In our recent report we have stressed the opinion of others besides ourselves that only the *absolute* figures which are based on all cases seen, not estimated, are of accurate value for comparison.

A comparative study of the late complications occurring after pure surgery or radiotherapy should be made. We know that complications occur some years after radiation therapy that are not necessarily of the nature of a metastasis or a recurrence, which may result in hydronephrosis, intestinal obstructions or pelvic pain. If such complications do not occur so frequently in pure surgery, we should know it.

We believe that our present results show that considering the lower primary mortality and the palliative value, radiotherapy offers the best for the great majority of these patients, as they otherwise must have the benefit of special technical surgical skill necessary to do a proper Wertheim operation.

But however we look at it, Mr. Bonney's figures are remarkable and show that a master surgeon trained in the Wertheim technic is essential to produce such wonderful results. His study of the gland involvement makes his classification of the extent of the disease far more accurate and valuable than is possible by those using radiation therapy alone. We must all admit that those cancer patients who have come under the skillful hands of Victor Bonney were fortunate indeed and have had as good a chance of recovery from this dread disease as was possible in any clinic, whether surgery or radiation therapy is employed.

DR. HOWARD C. TAYLOR, NEW YORK CITY.—There has been a tendency here among gynecologists and particularly among radiologists to think that irradiation is today the only treatment for carcinoma of the cervix uteri, that any advance in the treatment of carcinoma of the cervix uteri will be along radiologic lines, and that operative treatment no longer has any place in the treatment of any of these cases. This is wrong, as has been shown by Mr. Bonney's paper and the discussion of it. I do not know what the future treatment of carcinoma of the cervix uteri will be. It may be a combination of irradiation and operation. It may be operation for some cases and irradiation for other types. There is one point, however, about which there must be no question. It is a gynecologic problem. We as gynecologists have worked hard on this problem. Advances have been made by our work, and we must not yield it to the radiologists nor to cancer clinics.

DR. KARL H. MARTZLOFF, PORTLAND, OREGON.—It is interesting that the finding of carcinomatous lymph glands by Mr. Bonney in approximately 40 per cent of his operative material corresponds closely to the observations of Schottländer and Kermauner on Rosthorn's material and those of Weibel on Wertheim's material. The analogy ends however when one compares the 25 per cent incidence of five-year cures which Mr. Bonney has achieved in the gland-involved group with the experience of others in the same type of patient. This difference is forcibly emphasized when one contemplates the incidence of five-year cures obtained by Wertheim, Rosthorn, Bumm and Cullen's clinic which amount to 10.6, 4.1, 15.4, and 7.1 per cent, respectively. In fact the figures of Wertheim are based on patients who survived the operation and are therefore not entirely comparable.

Mr. Bonney's ability to salvage 25 per cent of his patients who had a carcinomatous lymph adenopathy, therefore, represents one of the outstanding achievements in the history of the surgical treatment of cancer of the cervix uteri.

I have been deeply interested for some time in a consideration of the subject which has for its purpose the justification of lymph gland removal in the operation for cancer of the cervix. Theoretically the procedure is logical and Mr. Bonney's

experience apparently offers practical proof of its value. However, it is obvious that in both groups of patients where extirpated lymph glands do or do not show cancer both may develop fatal recurrences and some of these undoubtedly represent lymph gland metastases. It is informative to note the incidence of fatal recurrence during the first two years after operation in Mr. Bonney's two groups of patients. In round numbers, this amounted to 32 per cent of those who had glandular involvement and 19 per cent of those without demonstrable involvement. This comparative difference is fairly uniformly maintained throughout the five-year period.

If one combines the primary operative mortality of 20 to 23 per cent, and the fatality from recurrences, during the first two years after operation among the patients with cancerous lymph glands, there is revealed a total mortality for the first two years of 55 per cent, and on the five-year basis this amounts to 69 per cent with a 24 per cent salvage.

A similar consideration of Mr. Bonney's patients who did not possess demonstrable lymph gland involvement reveals a total mortality for the first two years of 31 per cent (11.8 per cent primary mortality and 19 per cent fatal recurrences). On the five-year basis this comes to 40.1 per cent while the operative salvage reaches 51.3 per cent.

The difference is striking and I offer it because it is more or less lost sight of in Mr. Bonney's composite experience of an approximate 14 per cent operative mortality and a 39.6 per cent five-year rate of cure.

I have long doubted the wisdom of regional lymph gland extirpation in the abdominal operation for these tumors, because the high primary operative mortality, and the high incidence of early recurrence where lymphatic metastases have occurred seem to have robbed this procedure of any particular advantage it may appear to have possessed. While this point of view appears to be confirmed by Wertheim's incidence of 38.4 per cent five-year cures and an 8 per cent primary mortality following his abandonment of routine lymph gland removal, it appears to be even more strongly substantiated by the experience of those who are now practicing the radical vaginal operation where no effort is made to remove lymph glands. Here Peham and Amreich report a 3.6 per cent operative mortality and 48.7 per cent five-year cures; Adler reports 42 per cent cures (leaving out of consideration his experience with postoperative radiation) with a 3.8 per cent operative mortality, and finally Stoeckel, according to Schilling, has had a 4 per cent primary operative mortality with 58 per cent five-year cures in 150 cases.

In view of the foregoing it is still difficult for me to reconcile myself to the continued application of the ultraradical phase of the Ries-Clark operation for cancer of the cervix uteri, and I would appreciate knowing on what basis Mr. Bonney justifies the continuation of the effort at lymph gland extirpation.

DR. WILLIAM P. HEALY, NEW YORK CITY.—Mr. Bonney has told us that 44 per cent of his operable cases showed lymph gland involvement. It would be interesting to know whether cancer was present in those glands. If so, we must accept it as a fact that we cannot hope to salvage more than 50 per cent of the cases by radiation because radiation as we understand it today certainly does not cure cancer that is in the lymphatic glands at any distance from the cervix.

In the last series of any size that I reported from the Memorial Hospital of New York, a series of 1,600 cases of cancer of the cervix, we had a 46 per cent salvage in our operable cases. When you consider the lymph gland involvement, that is getting very near the top.

I would like to endorse Dr. Taylor's statement in regard to the gynecologist not giving up the treatment of cervical cancer or any other form of cancer in the genital tracts. If, however, it is decided to treat the disease it should be done as Dr.

Schwarz and others are doing, by developing younger men to be efficient in the treatment of cancer and not attempting to do both the surgical and the radiologic work because one cannot do them both well.

MR. BONNEY (closing).—I am not against preoperative irradiation. Some very remarkable results have been obtained by it; by Schlink of Sydney, for instance. What prejudiced me against it in the earlier days was that cases were sent us as having been rendered "operable" by radiation. These cases were very difficult ones. The radiation seemed to have destroyed the patients' resistance, besides causing dense fibrosis. I arrived at the conclusion that these cases would have been easier if radium had not been employed. An advantage of the course I have pursued is that my treatment has been purely surgical, whereas if I had used preoperative radiation the results would have to be shared between surgery and radiation.

As to preparation on the table, after trial of various antiseptics in the past I have for many years now limited myself to simply packing the vagina with gauze soaked in "violet green."

I agree with those who say that this is surgery's limit. We can go no further in surgery I am sure, whereas radiation has still no doubt an expanding future before it; but I do feel that the further progress of radiation depends on finding a method of destroying carcinoma in the regional glands. When this is achieved radiation will entirely supplant surgery. The fact that at present surgery can deal with these involved glands gives it a superiority over radiation.

What Dr. Taussig has said about iliac lymphadenectomy is very interesting because several of my colleagues and I have carried out the operation in suitable cases, but unfortunately I have not been able to keep in touch with all of my patients on whom I have performed this operation. The difficulty of keeping in touch with patients in my country is very great indeed. My Wertheim figures have been a purely personal matter with me, and even to obtain the figures that I have has been a big task. London is very large, patients shift around from place to place, and it is impossible to avoid losing touch with some of them. Follow-up departments are being established in our hospitals, and the men who come after me will find things easier in that respect.

What Dr. Ward said with regard to growths returning after ten years is very interesting. I have not personally seen a case. There is moreover no reason why a patient who has had Wertheim's operation should not develop an independent growth at some subsequent period. In that regard I cannot help noting what a large proportion of my cases of Wertheim's operation have had carcinoma operations in some other region of the body, either prior to or subsequent to my operation, and this suggests that certain persons have a special tendency toward carcinoma. Certain of these patients who have apparent recurrence after ten years really have a brand new growth and not a recurrence.

With regard to what Dr. Martzloff has said about glandular involvement, perhaps the difference in figures is explained by the fact that I have removed the regional glands in every case, no matter how early the primary growth, and they have all been examined microscopically. Wertheim on the other hand removed the glands only when they were definitely enlarged. I do not think it is so much the removal of the glands that increases the severity of the operation, but the advancement of the primary growth that accompanies the gland involvement.

One cannot look into the future, but I think it is quite possible that we shall one day see the end of surgery as a treatment of carcinoma of the cervix. There is, however, one advantage in operating over irradiating, and that is that you can keep the patient in absolute ignorance of her condition. She is told that she is bleeding and she is operated upon; she has no idea of what is the matter with her. She gets a recurrence and does not know what is the matter. She dies not knowing what is the

matter. The worst feature about irradiation in our country is that from the moment you start the treatment the patient becomes aware she has carcinoma, and though you may cure her physically, it takes a long time to cure her mentally. Patients who know they have had carcinoma and then get recurrence are distressing to watch. The return to radiation; the gradual realization of its failure, and the dread specter closing around—this is heartbreaking.

Finally there is this to be said for the operation; namely, that apart from its effect on carcinoma of the cervix, it has been and still is a great educational factor in gynecology, and it has raised the reputation of gynecologic surgeons in the opinion of surgeons in general, for the procedure is the most difficult of all surgical procedures. It has taught us the anatomy of the pelvis in a way that no dissecting-room preparations could possibly have taught, and it has enlarged the surgeon's vision, so that though in the future we may quite possibly see it replaced by a treatment more efficient, its disappearance from the field of gynecology will not be an entire gain.

**11. Physiologic Changes Occurring in the Urinary Tract During Pregnancy.** Drs. J. Mason Hundley, Jr., Henry J. Walton, John T. Hibbitts, Isadore A. Siegel, and C. Bernard Brack, Baltimore, Md. (By invitation.) (For original article, see page 625, November issue.)

#### DISCUSSION

DR. FREDERICK H. FALLS, CHICAGO, ILL. (by invitation).—In 1923 I pointed out that the dilatation of the ureter occurring in pyelitis of pregnancy was not a permanent change but rapidly disappeared after pregnancy was terminated. I was convinced by a study of autopsy findings in the ureter from a patient with pyelitis showing round-celled infiltration among the muscle bundles that the changes produced by the inflammation were not the cause of the dilatation since they would rather produce contraction. I also felt that the inflammation itself would irritate the ureter to spasmodic contraction rather than produce dilatation.

We have recently been able to show by means of the method shown yesterday by Adair, in studying the action of ergot derivatives, that an extract of the corpus luteum will completely inhibit the stimulating effect of 1 c.c. of obstetric pituitrin on the seventh day postpartum uterus when given hypodermically in one rabbit unit dose. We have also shown that this substance is valuable in the prevention of habitual and threatened abortion.

Kaltenschnee in 1911 showed that ureteral peristaltic waves were retarded in pregnant women and averaged 17.3 seconds longer interval between contractions on the affected side in pyelitis cases. This would seem to show that there was some interference with the normal stimulus to ureteral peristalsis during pregnancy.

Our explanation of the dilatation therefore would be that the antipituitrin action of progesterin probably plays an important part in the relaxation of the ureter. Estrin, on the other hand, we believe can play very little part except through production of the hypertrophic changes in the sheath of Waldeyer, which, as pointed out by Dr. Hundley, does not explain the position of the dilatation.

As noted by Dr. Hundley, we find in our experiments with this hormone in the human uterus that its chief effect on motility seems to be to sensitize the uterus to pituitrin. One would expect this action therefore to increase the tone throughout the ureter unless we assume that the hypertrophy of the musculature at the lower end of the ureter responds so much more vigorously to the sensitizing effect of the estrin.

In the large fibroids one could explain the relative lack of dilatation by the fact of their relatively slow development, giving chance for ureteral hypertrophy and accommodation and by the fact that in such cases there is no change in the endocrine system corresponding to the pregnant state, by which progesterin or other antipituitrin-like substance would be elaborated.

The position of the dilatation and its right-sided preponderance makes me feel with Dr. Hundley that pressure plays some rôle in producing the dilatation. However, the method of ureteral decompression as described in the paper is open to the serious objection that the long-continued presence of an indwelling catheter, plus repeated lavage of the pelvis with 1-1,000 silver nitrate solution, might stimulate ureteral spasm and thus bring about decrease in size. In order to be convincing, one would have to show that such procedure did not produce contraction of the normal or dilated ureter in nonpregnant women.

DR. GUY L. HUNNER, BALTIMORE, Md.—In 1925, in this JOURNAL, I reported some observations on cases of pyelitis in pregnancy and on cases of multiple abortion apparently due to renal insufficiency. In some of the latter class, one finds that after dilatation of bilateral ureteral stricture and restoration of better renal drainage, the patient who has had multiple abortions will carry through to term in subsequent pregnancies. Concerning pyelitis of pregnancy one cannot view a series of ureterograms, such as Dr. Hundley has shown, without marveling that any of these patients get by without developing pyelitis, yet we know that most of them do. Even in the comparatively few who develop pyelitis, many clear up spontaneously, as do many nonpregnant victims of pyelitis, simply by the routine of ten days in bed, proper posture, and forced fluids. Some ascribe these cures to the drugs given, but it is probable that rest, posture, and increased fluid intake, all of which promote better drainage, are the deciding factors. It is probable that in most of these pregnancy cases the drainage is not as sluggish as the ureterograms showing wide dilatation would seem to indicate, because of the muscular hypertrophy existing along the entire tract, especially in the lower portion, or in the sheath of Waldeyer. This general hypertrophy must accelerate propulsion of the urinary stream in spite of various external pressures, and I think it reasonable to suppose that the extra hypertrophy about the lower ureter may, by virtue of its stronger peristalsis, act as a suction pump to vacuum-clean the upper tract. These defense mechanisms seem adequate in most instances and most pregnant women escape pyelitis. As stated before, many of those who develop pyelitis are, with a little help, capable of spontaneous recovery. Those who do not recover spontaneously are often referred to the urologist. Adequate methods of investigation will show that practically all of these have ureteral stricture. In spite of the pregnancy most of them clear up promptly under treatment, by dilatation of the strictures, in addition to the simple methods which have failed until this further aid to good drainage is employed. In some the infection may persist until after the delivery, but the improved drainage results in cessation of fever and other signs of toxemia and enables the patient to carry to term.

Some indications in the patient's former history that invite investigation for the possible existence of stricture are the following: (a) a history of pyelitis in any previous pregnancy, (b) a history of a previous pyelitis attack in the current pregnancy, (c) a history of pyelitis at any former period of the patient's life, (d) a history suggesting the presence of stricture before the patient became pregnant, such as the combination of headache, backache, gastrointestinal symptoms, pains in the pelvic region, and urinary tract disturbances, no adequate cause having been found for these symptoms.

The author quotes Carson's pioneer work in which he found definite inflammatory stricture in 3 of 16 autopsies on pregnant women. Carson's explanation of these

strictures was that the pressure effects of pregnancy led to stasis with secondary infection of the urine, and consequent invasion of the ureteral wall resulting in local areas of stricture. My experience leads me to believe that such individuals probably had ureteral stricture before they became pregnant and that the stricture was a prominent factor in the subsequent urinary infection during pregnancy.

Pyelitis in the early weeks of pregnancy, especially if difficult to control, should arouse the suspicion of stricture. In testing for stricture in any period of pregnancy one must often employ larger preliminary bulbs than are used on the nonpregnant individual, because of the softened succulent character of the urinary tract tissues so well described by Hundley. Exceptions to this rule exist and at times the stricture areas are so dense as to mold down our smaller wax bulbs. To neglect the diagnosis and treatment of stricture, when it is present, is subjecting the patient to increased danger of future pyelitis attacks, or even more serious renal complications, as well as jeopardizing the general health.

**12. Recent Advances in Hysterography.** Drs. Thomas O. Menees, and J. Duane Miller, Grand Rapids, Mich. (By invitation.) (For original paper, see page 590, October issue.)

**13. Experiences With Amniotin in the Treatment of Gonococcal Vaginitis in Children.** Drs. Richard W. TeLinde, and James N. Brawner, Jr., Baltimore, Md. (For original article, see page 512, October issue.)

#### DISCUSSION

DR. CHARLES A. BEHNEY, PHILADELPHIA, PA.—The possible disadvantages of any new method of treatment should be considered. These preparations are uniformly expensive. They have been observed to cause changes in the secondary sex organs and Loeb, Engle, Selye, Collip and others have demonstrated carcinogenic properties in estrogenic substances when administered to animals experimentally. The shorter period of treatment required by this method by the use of estrogenic preparations, especially when the patients are hospitalized, more than compensates for the added cost of the preparations employed. Since vaginal application appears to be the most satisfactory method, there should be no difficulty in having the suppositories inserted by a trained nurse or some intelligent member of the child's family. If the hormone could be incorporated in an oily paste, dispensed in a collapsible tube with a suitable nozzle, the treatments would be simplified.

When one considers the short duration of administration required and the small dosage given as compared with these factors in relation to the experimental studies with small animals it becomes evident that the danger of carcinogenic activity is extremely remote and more theoretical than real.

The authors have suggested that recovery might be hastened if this treatment were supplemented by other measures. There is some danger that in cases where the hormone is injected under the skin there may be a great temptation to neglect to perform a careful vaginal examination in all instances. Dr. John Mitchell, of the Pediatric Service of Bryn Mawr Hospital, cites a case which illustrates the importance of thorough examination for every patient regardless of the treatment employed. This child had received large doses of amniotin hypodermically over a long period of time without improvement. The child was finally anesthetized and to his surprise examination revealed a hairpin in the vagina. After removal of the foreign body, prompt recovery ensued.



DR. THOMAS B. CARROLL, PITTSBURGH, PA.—Amniotin is certainly giving results that are very gratifying. The ease with which it can be administered is pleasing to the doctor as well as to the patient and is one of the principal recommendations. To be able to apply a treatment that can be more or less successfully carried out by the nurse or the mother decidedly recommends it. I am very much pleased and impressed with the results secured, for certainly the early administration would naturally have been attended with failure.

I usually expect very little of those preparations that have to be administered by mouth, and often not very much more from those which are administered hypodermically. The preparation in oil seemed to be attended with better results than that with ethylene glycol. Perhaps in the latter preparation there might have been some change brought about which was not occasioned by the use of oil and therefore gave the preparation a better chance. However, it is of very little importance to consider the various merits of the two preparations when one can get better results by the use of the suppository. The suppository is an age-old means of applying medicine of various sorts. So often does it fail that we give it little cognizance but here it seems to have redeemed itself.

There is only one new element that enters into the suppository and that is the vehicle that is used. I believe the preparation was made with glycerin. It is quite interesting to observe that with the glycerin there were no systematic reactions apparently, and I am disposed to wonder whether or not it was absorbed. If the preparation were absorbed in the vaginal canal there should be some reaction and it occurs to me that perhaps the amniotin was negligible, that it may possibly be that the glycerin alone so far as its superior result is concerned might have been responsible for the results attending the use of the suppository. I wonder if that would not be an enlightening thing if Dr. TeLinde would treat a series of patients, using the glycerin suppository alone in some and the amniotin preparation in others. Glycerin does not offer very much hope as far as the treatment of gonorrhea is concerned, but it has not been tried in this connection. Glycerin has certain properties that may render it helpful to this pathologic process. It may be that the advantages of the suppository treatment lie simply in the vehicle and not in the manner in which the amniotin is being introduced.

DR. ROBERT M. LEWIS, NEW HAVEN, CONN.—Since presenting to this Society the subject of the treatment of gonorrheal vaginitis with follicular hormone, two years ago, I have had the opportunity of acting as consultant in the treatment of these cases in Dr. Charles Hendee Smith's wards in Bellevue Hospital, New York. Dr. Helen Owen was in direct charge of the work. Although our results have not been as dramatically successful as Dr. TeLinde's, they have on the whole been highly satisfactory.

Of 61 patients treated with ethylene glycol amniotin, 48 have apparently been cured. Three cases were failures and 10 recurred. Like Dr. TeLinde, we found that even large doses of amniotin given orally produced no physiologic change in the vaginal mucosa. I have seen the desired reaction resulting from the oral administration of theelol in a few cases. A few cases of chronic vaginitis, not gonorrheal, have been treated and responded as well as did gonorrheal infections. Three hundred rat units of amniotin (ethylene glycol preparation) seemed the optimal daily dosage to effect vaginal changes. We did not try amniotin in oil.

Several cases of my own were treated with vaginal suppositories containing theelin, 50 R.U. each, twice daily. Of these, the first three or four did well. Subsequent cases failing to respond, we gave up the method believing that our suppositories had deteriorated. Dr. TeLinde's method of using gelatin capsules in the vagina is obviously an enormous improvement over the use of hypodermics.

Dr. James R. Miller reports treating 62 cases of gonorrheal vaginitis with follicular hormone (theelestrin) in his clinic and practice in Hartford. Of these only 8 resulted in failure.

In our series at Bellevue, 3 cases were of from six to twelve months' duration before receiving amniotin. Two had long-standing gonorrheal infections of from one to two years, and two more of two to five years' duration. These were all cured with amniotin. Cases of long standing appear to respond more quickly and favorably than do recent, florid infections.

Including Dr. TeLinde's report, we now have records of some 200 cases of gonorrheal vaginitis in girls treated with follicular hormone, the great majority of them successfully treated. In no case has the treatment caused any harm or injury. In not a single one has bleeding from the uterus followed when treatment was stopped. Apparently only brief transient alterations occur like the conditions always found in the vagina and breasts of the newborn female child. The many layers of vacuolated cells which make the vaginal mucosa of the parturient woman and newborn child histologically alike are artificially produced by administration of theelin. These many layers of cells may well be a natural protective mechanism against infection.

One must remember that although standardized, the preparations of estrin put out by the different firms vary in their effects. It is necessary to know the preparation that one is using and to administer enough to obtain the desired change in the vaginal mucosa. This can be measured best by biopsies along with microscopic examination of vaginal washings. The amount of estrin required to produce vaginal change in one individual may be insufficient to produce it in another. In some of our cases persistent rectal or urethral infections have been troublesome, reinfesting the vagina after it was apparently entirely clear of gonococci and discharge.

DR. NORMAN F. MILLER, ANN ARBOR, MICH.—We have from 6 to 20 of these children under treatment most of the time.

There are two inquiries I should like to make: the first concerns the criteria for cure. Many of our patients come from long distances, hundreds of miles, and we cannot discharge these patients until quite certain of cure. Consequently we have laid down a rule that each patient shall have three consecutive negative smears at weekly intervals following cessation of treatment. Even so some recurrences develop.

The second point is the matter of urethral infection. In our experience the gonococcus may be eliminated from the vaginal tract by the method discussed, but we find the occasional urethral involvement persistent and unresponsive to this type of therapy.

DR. FREDERICK J. TAUSSIG, ST. LOUIS, MO.—We apparently have in our hands a therapeutic agent that is effective in the treatment of gonococcal vaginitis. Is it not important now to give more thought to the prevention of this condition? When we consider the frequency of this infection in young girls it seems to me that we have neglected this phase of the subject. Twenty years ago I became convinced that one of the most common means of spreading this infection is in the early years of kindergarten and grammar school life when children congregate in large numbers in schools where the lavatory facilities are not properly supervised. I think that the careful supervision of girls at that time is a matter that should receive more attention.

I would like to ask Dr. TeLinde two questions: first, has he tried this form of treatment in vaginitis of nongonococcal origin? Second, has he examined the cervix of these girls to see whether any changes occur in the epithelium of the cervix; or has he taken any biopsies that would indicate that such changes occur?

DR. FRED L. ADAIR, CHICAGO, ILL.—I would like to call attention to work Dr. Davis has done on the appearance of vaginitis during the period of second childhood. The changes in the epithelium were apparently the same following the use of amniotin. It usually takes from three to four weeks to build up the epithelium and the process of upbuilding recedes in three to four weeks again, and it can be rebuilt by the subsequent administration of amniotin. We use principally the hypodermic injection, usually of 100 rabbit units three or four times weekly and sometimes that is combined with amniotin suppositories.

DR. C. FREDERIC FLUHMAN, SAN FRANCISCO, CALIF.—The use of suppositories represents a definite advance.

It seems doubtful that the modifications induced in the squamous epithelium are sufficient to account for the improvement which results, and attention should also be directed to certain biological changes. The infantile vagina has a low acidity, a high glycogen content, and the bacterial flora is composed mainly of cocci. After puberty, the pH advances farther to the acid side, the amount of glycogen diminishes, and bacilli make their appearance. It is quite possible that such factors are of importance in the control of infections.

In 1932 I presented before this Society the results of an experimental study in rabbits, in which it was shown that the administration of estrin enhanced the reactions induced in the pelvic organs by trauma. This manifested itself by vascular changes and the appearance of large numbers of macrophages. Since these factors are of importance in controlling infections, it was suggested that estrogenic substances be employed in the treatment of pelvic inflammatory conditions.

A small series of adult patients with pelvic inflammatory disease has been treated with amniotin, each individual receiving from 3,000 to 15,000 rat units over periods of from six to fifteen days. Without going into details, it may be stated that this method of therapy did not seem to offer any great advantage over conservative methods of treatment. However, there was one important finding in that the administration of amniotin seemed definitely to influence pain. Of 27 patients in whom pelvic pain was a prominent symptom, 10 had complete relief, 13 partial relief, and 4 were uninfluenced, within a short time after the injections had been instituted.

DR. NATHAN SEARS, SYRACUSE, N. Y.—There is one phase of gonorrheal vaginitis in children that I would like to emphasize, namely the relatively frequent occurrence of an accompanying cervicitis. This seems to be the cause of chronicity. I would like to ask if the amniotin has the same effect upon the cervical epithelium as upon the vaginal epithelium.

A second question: Does he wait any time at all for the acute stage of vaginitis to subside before placing the suppositories in the vagina?

DR. TELINDE (closing).—Replying to the question as to whether the amniotin or the other ingredients in the suppositories are responsible for the cure, I am so convinced of the ineffectiveness of the chemical therapy, I cannot believe that a little glycerin and carbolic acid in the suppository would have any effect. Also the fact that we get the same effect with the hypodermic treatment (although not so consistently) proves to me that it is the hormone that is doing the work. The weak point in the therapy were the recurrences which we had, but all of the recurrent cases cleared up promptly when retreated with suppositories. Of course, the question of reinfection always comes up. One child came back with a recurrence, strongly denying that she had had any sexual contact, but she had an anal chancre.

Replying to Dr. Miller's question about infection of the urethra, we saw no clinical evidence of urethritis, although we did not take urethral smears. I think it is possible that the drug given in suppository form may have an effect upon the

urethra as well as upon the vagina. A castrated woman came to us a few months ago with a reddened area about the urethral meatus. The lesion was not a caruncle but seemed to be covered with atrophic mucosa. It was the source of a great deal of irritation in that region. After trying all sorts of things without relief we finally in an experimental way gave her some vaginal suppositories of amniotin. The epithelium of the reddened area became thickened and the redness and irritation disappeared. Of course, that was not a gonococcal condition.

Answering Dr. Taussig, we have made no biopsies of the cervix. It would be reasonable to suppose that the vaginal portion of the cervix covered with stratified squamous epithelium undergoes some change as does the vaginal wall. We have no histologic data on this, however.

In regard to Dr. Davis' work, that is a problem which we ourselves have had in mind and the results are entirely in keeping with the laboratory work done by Hartman on castrated monkeys. The atrophic vaginal epithelium of the castrated monkey is just as demonstrated in the postmenopausal women. After all, in senile vaginitis we have much the same problem as in these children. The thin senile vaginal mucosa often has minute ulcerations allowing the vaginal flora to infect the subepithelial tissues. Thickening of the epithelium may be all that is necessary to allow the vaginitis to get well spontaneously.

We have had no experience with nonspecific vaginitis in children but it is our intention to try amniotin in some of these cases.

**14. Ovary-Stimulating Factors and Antihormones.** Dr. C. Frederic Fluhmann, San Francisco, Calif. (For original article, see page 584, October issue.)

#### DISCUSSION

DR. MORRIS A. GOLDBERGER, NEW YORK, N. Y. (by invitation).—Dr. Fluhmann has demonstrated a species variability of the inhibiting factor; that is: rats sensitized against human pituitaries would only inhibit ovary-stimulating extracts from human blood, and were ineffective to extracts from sheep pituitary. This brings up the question whether this phenomenon is really due to antihormones.

Is it not possible that the inhibitory effect ascribed to an antihormone is due to species antibodies? Anterior pituitary extracts prepared thus far are not entirely free of proteins. The infinitesimal amount of protein necessary to stimulate antibody formation is well illustrated by the work of Dr. Sabin, who, in trying to produce antibodies from tubercle bacilli grown on carbohydrate media, was unable to free them from proteins in the millionth dilution, and had produced antibodies against these proteins.

That there is a species variability in reaction to hormones is well known. Mice are more sensitive to the follicle stimulatory fraction than are rats, while rats, with more than double the weight of mice, give a greater response to pregnancy urine extracts. Monkeys, when injected with pregnancy urine extracts, show no follicular growth in their ovaries. Geist has shown the same is true of human ovaries by injection of aututrin "S." These differences in response may be due to the ovary which Smith calls the end organ. Ferold, Hisan and Evans attribute this difference in response to the amount of circulating prepituitary hormone in the individual, which augments or activates the extract injected.

Variations in reactivity of the ovary in the same species to stimulating factors found in pregnancy urine have been apparent to us for some time. In September we reported that in over a thousand Friedman pregnancy tests done in duplicate at our laboratory, we found that 3.5 per cent of the rabbits were refractory—that is, one rabbit would be positive showing blood spots, and the other rabbit negative

showing normal ovaries. In doing the test in duplicate, we have been able to reduce the errors from 5.5 per cent to 0.5 per cent. In the last 265 Friedman tests, we have also observed 6 instances ( $2\frac{1}{4}$  per cent) in which one ovary in the same rabbit showed blood spots while the other was negative.

The variation in the reactivity of the ovaries in the rabbits observed by us may be due to a difference in the responsive capacity of the ovaries rather than a difference in the potency of the pregnancy urine or to an antihormone. This would explain the reaction of only one ovary in the same rabbit. Aging processes of the ovary decrease their capacity to respond. This is well shown in the ovaries of women in the menopause. Here there may be large amounts of follicle stimulating and luteinizing hormones (as recently shown by Frank), yet no follicle ripening occurs.

To sum up: The evidence so far shows that under certain conditions, refractiveness to a given quantity of hormones may develop, but the explanation as yet is by no means convincing that this is due to a species antihormone. The possibility exists that the prepituitary hormone actually contains protein as part of its molecule—in which case this would be understandable. Personally, I prefer to adhere to the opinion of those who defer the final interpretation until a crystalline prepituitary hormone has been obtained.

DR. KARL M. WILSON, ROCHESTER, N. Y.—Isolation of the ovarian and other hormones has led us to hope for a great deal from the therapeutic standpoint—probably we have been hoping for too much. The demonstration of the fact that the body can develop more or less specific antihormones adds another phase to an already difficult and complex problem. Dr. Fluhmann offers the suggestion that there might be some therapeutic value in the antihormone. Where an individual's symptoms are the result of an overproduction of a certain hormone, theoretically at least, if the development of a specific antihormone could be stimulated in the body, the symptoms should be overcome. Again theoretically, the converse might well be true. That is to say, if we can definitely demonstrate that a patient's symptoms are due to the lack of a certain hormone, and she is given that hormone in a therapeutic manner, this may be followed by relief of the symptoms. However, if given in sufficient quantity and over a sufficient length of time, administration of this hormone might well result in the development of an antihormone, thereby nullifying the results of previous treatment.

For the present at least, this, of course, can only be considered on theoretic grounds, and it is impossible to make specific statements from the standpoint of therapy. Along this line, I have in mind a patient whom I have observed for the past one and a half years who has been suffering from excessive uterine bleeding which we believed due to an underproduction of progesterin. During the past year she has been receiving hypodermic injections of progesterin with extraordinarily satisfactory results until a couple of months ago, but since that time it has failed to stop the bleeding. I do not know what that means—whether the administration of progesterin stimulated the overproduction of an already too abundant amount of estrin, or whether she developed an antihormone which nullified the effect of the progesterin therapy. All this offers an interesting problem to speculate on, and it may have very distinct possibilities.

**15. Some Newer Aspects of Reproductive Physiology.** Dr. Emil Novak, Baltimore, Md. (For original article, see page 495, October issue.)

#### DISCUSSION

DR. ROBERT T. FRANK, New York City.—The first time that I brought up the subject of endocrinology in this Society was twenty-four years ago. Times

have changed since then. At that time we knew only of the corpus luteum as the active sex factor. Today we have to consider the pituitary, the follicle elements, the corpus luteum, and now from the work that Dr. Novak refers to, possibly a sex center. Formerly his views and mine differed much more than they do now. In crude analysis he is a romantic in medicine, I am a realist. His function is that of an observer in an airplane up in the air over the battlefield to see what is going on below, to get an outline of the general action; mine has been in the trenches. I have not been alone. I have been helped by an enthusiastic group of collaborators. However, my outlook and his have naturally been at variance.

I will refer to only a few of the achievements that Dr. Novak has emphasized. As far as anovulatory or pseudomenstruation is concerned, I think that phenomena can be accepted but with some reservation. Schroeder and Geist first pointed out this form of abnormal bleeding. Others (Hartman) have shown that a menstrual cycle can occur without a corpus luteum forming. The deductions, however, made from such a technic as suction curettage—I think the term suction biopsy would be preferable—must be accepted with great reserve unless the result is positive. If you find a secreting area of endometrium you may say that the evidence favors ovulation. If, on the other hand, you get a negative result, I would even distrust a thorough and complete curettage, if negative, unless such sections had been very thoroughly examined. Therefore, one must be warned against drawing conclusions from a single section of the uterus because if you remove the uterus you may find quite different cyclical changes in different parts of the endometrium.

That removal of the corpus luteum produces bleeding was brought out in 1905 (Fraenkel) but that it should be made a determining factor in bleeding is not warranted because, as was agreed after a long controversy, the human corpus luteum also secretes large quantities of estrin, so we need further clarification before this point is settled.

As Dr. Novak emphasized that he wanted to bring out the newest advances in endocrinology, I believe it a good opportunity to mention a few of our own laboratory discoveries which are in press, and give you some information in advance. By improvement of technic Dr. Salmon and I have obtained the concentration of the prepituitary factors in the blood and in the urine quantitatively much richer than before, with astonishing results. The surprising thing is that heretofore we have considered the pregnancy reactions, namely the Aschheim-Zondek test, as strictly associated with pregnancy. Our findings disprove this.

Dr. Goldberg and I have also recently improved our female sex reaction in the blood and urine to such an extent that we can obtain a positive reaction with 40 cm. of blood, even immediately after the menses. Though our quantitative results are greater, we are glad to report that so far as the graph of the cycle is concerned there has been no change. Geschickter and Lewis, as Dr. Novak told you, describe large quantities of sex hormone in adenomas of the breast and in fibroids. Consequently it became necessary to look for controls and we have selected the psoas muscle which is readily obtained at autopsy and we found that the amount in the psoas muscle is as great or greater than the amounts that they found in tumor tissue. This leads to two deductions: first, that the mere presence of estrogenic substances is not an indicator of action; and second, that very possibly this elusive estrogenic factor which disappears out of the blood may be stored as glucose is stored, perhaps in the muscles, possibly in other tissues.

The first suggestion offered by Dr. Novak is that of the relation between the sterol substances, as possessing carcinogenic qualities, and the hormones. May they or their derivatives not be that thing which makes it necessary for the embryonic epithelial cell to split prematurely and then invade? The similarity, then, chemically, between these substances and the hormones naturally suggests the theory

that the hormones may be factors in tumor growth. For a number of years I have thought of the irritative factor in the production of cancer as much more probably a chemical than a mechanical one.

The relation between the hormones, especially those of the gonads, is another suggestive thought in connection with this work. Also the relation between the sex glands and the neurovegetative system which was brought out some years ago by Maranon.

Of most interest to me is Dr. Novak's discussion of anovulatory menstruation. It has been my good fortune to provide the material for a histologic study of the uterine mucosa, both in menstruation and otherwise, and to follow the work done by Bartelmez at the University of Chicago. I have also seen the development of this work which has been finally published, at least in part, and we came to the conclusion some years ago from the histologic examination of the mucosa alone, that there could be menstruation without ovulation. It may not have been presented in such a way as to convince everyone, but at least we felt sure ourselves that a woman may go on menstruating even if the follicle did not rupture and there was no corpus luteum. This may be due, in part at least, to an absence of the ferment in the liquor folliculi, claimed by Fränkel some years ago as an aid in breaking down the overlying structure. Hence, if the follicle were deficient, for some reason or other, in this ferment, this might help to explain why the follicle does not rupture and a corpus luteum result.

I feel, however, that the examination of the corpus mucosa by Dr. Novak's aspiration biopsy would be effective in a certain number of cases only where the changes were definite. Our experience is that these changes vary, especially in association with a cystic follicle as is apt to be the case, and that these changes show a gradation which is not always definite enough. It is a question whether in every case it would be possible by this biopsy to determine if the menstruation is anovulatory or not. Further, anovulatory menstruation is undoubtedly a factor in certain cases of sterility. There is not time to go into this at length but it occurs to me that perhaps a sterility of this type might be an explanation of what we have called "biologic incompatibility."

DR. NOVAK (closing).—I believe that Dr. Frank is under a misapprehension as to the amount of tissue obtainable by our method of aspiration-curettage. We can easily remove as much as we like, even practically all the uterine mucosa, and this can be done almost always without anesthesia and with no great pain. In asking for serial sections, he is demanding an unreasonable criterion, and, I believe, an unnecessary one. By our ordinary laboratory technic the curettings are bunched and a number of sections taken at different levels. There is never any difficulty in recognizing secretory changes, even histologically, in the immediately premenstrual endometrium of the ovulating woman, so that differential staining is only confirmatory. Absence of secretory changes by similar criteria is, to my mind, to be interpreted as indicative of an absence of progestin and therefore of ovulation. I do not believe that the cutting of serial sections would alter our conclusions in any way.

Dr. Frank attacks the findings of Geschickter and Lewis at a vulnerable but not a very pertinent point. I fully agree that the mere finding of large amounts of estrogenic hormone in various tissues has very little significance. For that matter, these authors report finding large amounts of prolan in a large lipoma, though no one would ascribe any causative influence to this hormone substance as related to lipoma. But the actual production of neoplastic conditions by giving large amounts of estrogenic substance, as reported by the investigators quoted in my paper, is another story, and the one related to the present discussion.

I agree also with Dr. Frank's emphasis upon the quantitative factor in hormone relationships. I have repeatedly stressed this in the discussion of anovulatory menstruation. I do not believe, as Kurzrock seems to do, that prolan A is the ovulating factor, nor that prolan B is the one especially concerned, as some of the British investigators suggest. The evidence points to the fact that a rather delicate quantitative balance between the two principles is necessary for the occurrence of ovulation.

In my paper I have shown that an increasing number of gynecologists are encountering anovulatory menstruation in the study of sterile women, some much more frequently than we do. Some, indeed, report an incidence so high as to cast doubt upon the accuracy of histological study.

**16. Analysis of End-Results of Labor in Primiparas After Spontaneous Versus Prophylactic Methods of Delivery.** Drs. Albert H. Aldridge and Paul Watson, New York City. (For original article, see page 554, October issue.)

#### DISCUSSION

DR. CLIFFORD B. LULL, PHILADELPHIA, PA. (by invitation).—Dr. Aldridge stresses morbidity. I believe that this is important because from the many articles that I have read in lay magazines, it seems that the public know more about maternal mortality than we do. Therefore a discussion of morbidity rather than mortality seems to be in order. Since 1922 we have gradually increased the number of operative deliveries. I do not mean interference in obstetric cases, particularly in cases of abnormalities of the mechanism of labor, but rather an increase in the number of so-called prophylactic operations. We have just had the experience of observing a series of 1,600 patients who were given neubutal and scopolamine in fairly early first stage labor, and we have been particularly impressed with the decrease in the number of operative deliveries, such as version and midforceps, but have also of necessity increased the number of prophylactic forceps. It is almost always necessary to deliver these cases under light nitrous oxide anesthesia in order to keep them quiet on the table. We are fairly certain that the use of analgesia when used more extensively, will decrease the number of difficult operative deliveries. Our practice is about the same as Dr. Aldridge has outlined for you.

As to perineotomy, I am in accord with the practice of doing a central incision. Occasionally this will tear into the rectum, but as it is so seldom, I do not believe that it should deter one from using the midline. We do the perineotomy fairly early and remove the forceps from the head as soon as it can be controlled in the vulvar outlet.

Our handling of breech cases differs in that we extract a rather high proportion when the cervix is completely dilated rather than to allow them to go on spontaneously. We do this under general anesthesia. We are particularly careful not to give the patient partial anesthesia when part of the child is delivered, as we feel a partially anesthetized patient being delivered of a breech presentation very frequently gives rise to difficulty in the extraction of the head.

Our incidence of version has decreased very considerably during the past few years, particularly since we are using more analgesia.

We have not accepted the low cervical section as a routine procedure. When the operation is done at the time of election, we do the low classical; if the patient has been in labor, has been examined, or has ruptured membranes, we do the low operation. I believe, however, that in the last few years we have unquestionably given more cases a test of labor than we did previously. Our statistics are about the same as Dr. Aldridge's.



In discussing the question as to what undergraduate students should be taught, I, too, like to feel and believe that we should teach the students to do what we do, but it does not seem to me that the time has arrived as yet when the general use of prophylactic forceps should be taught to students who are going to practice obstetrics in poorly equipped hospitals or homes. In other words, the use of obstetric forceps as a routine procedure should be done in well-equipped hospitals and by men who have had special training. If we could teach the students to recognize abnormalities and complications, and teach them that the complicated case should be handled by the man particularly trained in this work, we would do a great deal to reduce obstetric mortality and morbidity.

DR. WILLIAM C. DANFORTH, EVANSTON, ILL.—A study of neonatal mortality recently made covering the work of the past five years cared for in the obstetric division of our service has indicated quite clearly, so far as our service is concerned, that the rather liberal use of outlet forceps by a staff of trained men does not increase fetal mortality or morbidity. A comparison of the cases delivered by outlet forceps shows that the result, so far as the infants are concerned, is somewhat better in the outlet forceps group than in those which were spontaneously delivered. It must be understood that this statement is sharply limited to outlet forceps cases. A moderate number of midforceps cases showed a sharp rise in infant mortality. It must always be understood that the liberal use of forceps delivery presupposes two things: first, that the liberality extends almost entirely to low or outlet operations; and second, that the operations be done skillfully. As the essayist has indicated, it is a procedure for the skillful obstetrician in a well-equipped hospital. An outlet extraction done with full knowledge of the mechanism of labor, the last portion of which the extraction is designed to replace, and with adequate understanding also of the technic of the forceps operation, is a highly innocuous procedure. This is not true of roughly or unskillfully done operations. It has seemed to us that the total sum of trauma to which the head is subjected is greater when the head is allowed to be compressed by a strong contraction against a rigid perineum than it is when a timely episiotomy is done and the head gently disengaged from the birth canal by outlet forceps. It also enables the obstetrician to perform incision of the perineum, if this is needed, deliver the baby, express the placenta and suture the perineum under one anesthetic, thus decreasing considerably the discomfort of the mother.

In the use of perineal incision, also, I find myself in agreement with Dr. Aldridge. Particularly in primiparas a timely episiotomy, done before the levator muscles have been separated by the advancing head, and followed by a careful repair, is far more effective in preserving a good perineum than an attempt to deliver without incision. In the latter event the musculofascial structures of the pelvic floor are likely to show a lesser degree of integrity eight weeks after labor. I am quite in accord with the essayist's statement that abnormal pelvis, faulty presentation and disproportion are far more active causes of neonatal trauma than properly done outlet forceps deliveries. The same is true as to maternal injury.

Our experience has quite clearly indicated that neonatal deaths during or after operative deliveries accomplished by the exhibition of greater force than is needed in the simple outlet forceps delivery in the majority of cases is caused by intracranial injury. Our efforts, therefore, have been directed toward decreasing as much as possible these more traumatic deliveries. To this end patients and analgesic agents contribute materially. The neonatal mortality in cases delivered by various procedures is indicated in the following table:

## EVANSTON HOSPITAL 4,924 CASES

	TOTAL DELIVERIES	FETAL MORTALITY	FETAL % MORTALITY
Spontaneous	2,456	17	0.69
Low forceps	1,826	8	0.43
Midforceps	161	8	4.96
High forceps (2 cases only)	2	1	50.00
Breech ext.	158	7	4.43
Version and ext.	102	10	9.80
Low cervical section	219	12	5.48
Total	4,924	63	1.27

DR. NORRIS W. VAUX, PHILADELPHIA, PA.—Coming from a Philadelphia Clinic which has always been considered radical in its care of these cases, this very interesting paper of Dr. Aldridge's strikes a pleasing note. At our clinic we are very prone to have a great many emergency cases. The mortality in these cases without adequate prenatal care is very striking when compared with those who have attended our prenatal clinic, where we do not consider prenatal care adequate unless a patient has made at least three visits. In our series in over four and a half years, there was a large proportion of cases which, apparently due to the economic distress, had very inadequate prenatal care, and in this group the fetal mortality was very high.

The fetal mortality in our clinic, based on a five-year period, showed 58 deaths in 182 cases of breech delivery, an incidence of 1 fetal death in every 3 breech deliveries. In 1,972 cases delivered spontaneously, there were 189 fetal deaths, or 1 in 10.5; excluding a number of tiny prematures which dropped into the vaginal canal in this group of cases delivered spontaneously, brings the incidence to 1 in 36.7 as compared to the fetal mortality incidence in those cases delivered by forceps application, which was 1 in 41.6. There were 31 deaths following cesarean section, a fetal mortality incidence of 1 in 10; in this group there were a large number of emergency cases as well as toxic cases.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—The papers plus the discussion have shown conclusively that mortality and morbidity may be reduced by the proper use of prophylactic forceps, limited to the skilled obstetrician in a well-appointed hospital.

MR. VICTOR BONNEY, LONDON, ENGLAND.—The paper is particularly interesting to me because there has been a very strong feeling against obstetric interference in our country and many well-known obstetricians inveigh against it. The reason is that the vast majority of women in our country are confined in their homes and are attended by the ordinary practitioner.

The paper bears out what I have always thought, that if the full gamut of surgery were applied to obstetrics much of the danger to the child and mother could be abolished. Unfortunately in England much of this work is not done under expert conditions. It would be difficult to get this practice applied in our country at large. We shall have to teach our students that, given expert conditions, it can be done advantageously but we must impress upon them that such practice is only justified where good conditions and expert knowledge prevail.

DR. J. C. LITZENBERG, MINNEAPOLIS, MINN.—This paper has done a desirable thing and that is to crystallize our ideas about the proper delivery of women, and about what is conservative and what is radical. It is not radical to do a cesarean section on a contracted pelvis through which the baby cannot go. It is not radical to do a high forceps when it is indicated. We have been doing this for ten years

in the University Hospital. It is not radical to do a midforceps operation when it is indicated. The low forceps is not to be classed with forceps operations in general as a radical procedure. I have been among those who have fundamentally condemned and still condemn the promiscuous employment of cesarean section, or ill-advised forceps operation, or version, but I have been compelled during this time to find out by experience that the outlet forceps application is a conservative procedure, a life-saving one for the baby in many cases.

We have already heard in this discussion from New York, Philadelphia, and Chicago and you are now hearing from Minneapolis that we have been thinking along similar lines and developing our ideas regarding the outlet forceps operation and the episiotomy. I agree with the method of doing an episiotomy, usually central, sometimes midlateral, and, in versions, laterally.

The mortality and morbidity in high forceps operations even in skilled hands are still high. The mortality and morbidity in midforceps is about half as high, but in skilled hands the mortality and morbidity are as low with the outlet forceps operation as in spontaneous delivery. When I use the term "outlet forceps" I mean application of the forceps really at the outlet, with the pelvic floor distending, and not their application when the head is only to the pelvic floor. We must make a distinction between "low forceps" when the head is on the pelvic floor and "outlet forceps" when the floor is distended and the head visible. The latter is a conservative procedure, the former is attended with almost the same dangers as "midforceps."

DR. JOSEPH B. DELEE, CHICAGO, ILL.—About fifteen years ago I brought before this Society a paper on the prophylactic forceps operation. I was not the father of prophylactic obstetrics in the second stage but I do claim, perhaps immodestly, that I was the accoucheur who delivered the idea. Prophylaxis in this field of obstetrics preceded me by many years. My teacher, Prof. Jaggard, taught episiotomy, which was heretical obstetric practice in 1889. The prophylactic forceps operation was proposed not on statistical grounds, but as the direct result of my own personal observation of thousands of cases and a study of the pelvic floor after delivery, in both living and dead women. I took the opportunity to make anatomical dissections of several women who died of hemorrhage or rupture of the uterus, immediately after death and I came to the conclusion that a spontaneous delivery usually causes more damage to the pelvic floor than an episiotomy and forceps. Some women will not tear. They will deliver nine- or ten-pound babies and the pelvic floor and bladder will be in good condition. If examined several years afterward you can hardly tell that they have had a baby, but those women are rare. There are a large number of women who will tear no matter how deep the episiotomy is made; it seems that the tissues have no resilience or elasticity whatever. Now, under my more or less empirical prophylactic forceps operation Dr. Aldridge has put a statistical basis.

It has been said that prophylactic operative measures should not be taught to young men to be practiced in the home. I have had an enormous experience with women delivered at home, covering at least 60,000 cases. Among the last 10,000 patients delivered in their homes by the Chicago Maternity Center, 12 women have died and only 2 might be chargeable to the service. This includes all patients sent to the hospitals and women who have had even one visit or only a telephone call to the Center. In the last 3,300 deliveries not one woman has died. The morbidity of these women has also been low in comparison with those delivered in hospitals, and a large number of prophylactic deliveries were done in these homes.

DR. ARTHUR H. BILL, CLEVELAND, O.—I have used prophylactic forceps routinely for more than twenty years. In recent years in the University Hospitals in

Cleveland there are delivered each year about 3,000 women by operative means. The reason we do this is because we are thoroughly convinced that we do not increase the mortality or morbidity in this way.

Some years ago Dr. Reyerast gathered together an extensive series of cases from my service delivered spontaneously and a similar number delivered by prophylactic means. The morbidity was no greater in cases where operative interference was resorted to. I believe that with proper prophylactic methods maternal mortality and morbidity are not increased. I think the fetal mortality is perhaps decreased.

Enough stress has not been laid upon the proper prophylactic methods. Very little has been said about when to interfere and about the cervix. Now all of these prophylactic methods should be in second stage deliveries. The minute the doctor starts to interfere before the cervix is completely dilated he is heading for trouble. The secret of our success has been largely due to the fact that we are very insistent upon allowing the first stage of labor to take its full course, except in emergencies when we do not hesitate to interfere either by the low prophylactic forceps or by the correction of abnormal positions.

A short time ago I reported before this Society a series of 500 occipitoposterior cases which I had personally delivered by operative means, and another series of 500 posterior cases delivered by operative means by the resident staff. Since then I can quote a series of 200 consecutive posterior cases which I have personally delivered. All of these cases were carried through labor, painlessly from start to finish, delivered with complete anesthesia by operative means, either by forceps rotation or by podalic version and with no mortality. Of the 200 cases there are 199 babies living today. The one which died was a case in which there were anatomical defects which were absolutely inconsistent with life. I simply quote these figures to show that prophylactic means can be carried out if done properly and at the right time. I again want to emphasize the reason why there is not success in a large per cent of these cases. It is because interference is done too early and resorted to when the cervix is not obliterated.

DR. THOMAS B. CARROLL, PITTSBURGH, PA.—Pittsburgh has arranged to compensate in a modest way the physicians and hospitals taking care of maternity patients who are on relief. There have been thus far some 6,000 patients delivered. The requirements for the care of these patients consists of a certain amount of prenatal care; they must receive eight prenatal visits where there is sufficient time; the urine must be examined, certain attention given during delivery, and a certain number of visits made following the delivery. About 60 per cent of these cases have been delivered in their homes, 40 per cent in the various hospitals. Up to the present time there have been 6 maternal deaths. In spite of practice by inadequately trained doctors, the mortality has been reduced to something like 1 in 1,000 deliveries. Out of those 6 deaths one was caused by self-induced abortion resulting in septicemia; another by her husband who came home late at night and kicked her into unconsciousness. This patient was taken to a hospital with separated placenta; cesarean section was done and she died. These deaths should not be attributed to the obstetric practice but to the lack of obstetric care.

17. Protein Stabilization in Preeclampsia and Eclampsia. Drs. Boyd Harden, W. S. McElroy, and R. R. Huggins, Pittsburgh, Pa. (For original article, see page 524. October issue.)

## DISCUSSION

DR. H. J. STANDER, NEW YORK, N. Y.—The present authors, in this thorough study, have corroborated the findings of Mendenhall and Smith regarding the use of heparmone in the treatment of eclampsia.

As to the second part of their paper, dealing with high protein diet, I am inclined to agree with their deductions. Strauss in a recent paper has attempted to show that a restricted dietary intake of protein in pregnancy may be actually harmful.

One of the main manifestations of eclampsia is water retention, according to the very old edema theory of Traube and Rosenstein. This may be due, in some measure, to the lowered osmotic pressure of the plasma proteins. There is general agreement today that the albumin fraction is lowered and the albumin-globulin ratio decreased. Strauss has also shown an increased venous pressure accompanying the lowered oncotic pressure.

High protein diet, therefore, may be of actual help in the treatment of this disease, on the basis that the osmotic pressure within the blood stream may be raised by restoring, in part at least, the concentrations of the various serum protein fractions. Could this be accomplished by the high protein diet, then there must of course follow loss of water, held in the tissues, in order that equilibrium may be maintained and such processes as osmosis and diffusion continue in the desired directions. Even in nephritis our dietary treatment is today toward high protein rather than low protein diet. I have never advocated the use of low protein diet in eclampsia and preeclampsia, but I have done so for nephritis. I am free to admit I may change my views.

DR. WILLIAM J. DIECKMANN, CHICAGO, ILL.—Dr. Huggins and his coworkers have stated that there is a significant decrease in the serum protein in the toxemias of pregnancy. They ascribe this decrease to an insufficient protein intake and/or excessive loss of protein in the urine. There is no doubt that if the serum proteins become markedly decreased edema may occur, but it may also subside without any increase in the serum protein concentration. The serum protein concentration in the toxemias rarely reaches the edema level. The most striking phenomena is that simultaneously with or shortly after delivery, or the death of the fetus, the patient shows clinical improvement with the serum proteins decreasing to a concentration less than that found at the height of the disease. If the decrease in serum protein is the cause of the edema and of the associated symptoms and signs, a blood transfusion or a transfusion of plasma protein should cure the condition. We have transfused toxemic patients without noting any improvement.

Another method of raising the serum protein concentration, or rather the colloid osmotic pressure, is by the injection of gum acacia solution. Hartmann has been able to keep children free of edema for as long as two years with repeated injections of acacia. Some of the children have eventually been able to produce their own serum protein and have recovered, while the others have ultimately died. We injected acacia solution into several eclamptic patients with phenomenal results, but we did not ascribe the clinical improvement to the increase in osmotic pressure but rather to the blood dilution.

It should be noted that most of the patients developing eclampsia have not been on a starvation diet. Furthermore, prenatal care, an essential part of which is proper elimination and proper diet, in the past two decades has lowered markedly the incidence of eclampsia. The decrease in the number of cases of eclampsia that occurred in the Central Powers during the War has been ascribed to the decrease in protein intake. During the period of the depression our dispensary patients are

all on a low protein intake because of the financial condition, and yet the number of cases of eclampsia has certainly not increased.

The essayists have stated that in eclampsia large amounts of albumin are lost in the urine. During the acute phase of the disease the concentration of albumin in the urine may reach 4 per cent or 40 gm. per liter; but during this period the volume of urine is usually only a few hundred cubic centimeters. In others words, the total excretion of albumin per twenty-four hours is well under 10 gm. per day, and as a rule it requires a loss of at least this much to decrease the serum protein concentration.

Dr. Huggins and coworkers have accumulated a mass of valuable data and should be commended for directing attention to the importance of nitrogen metabolism especially where there is a prolonged albuminuria. However, in view of these various observations, it does not seem reasonable to ascribe their reported results to the increased protein intake.

DR. HARDEN (Closing).—We will answer Dr. Dieckmann's question indirectly by stating that the effect of feeding maintenance amounts of protein does not necessarily result in elevation of the total protein of the plasma. Further, we have not observed high negative nitrogen balances in asymptomatic albuminuria.

The formed elements of the blood in each of these cases rested in levels approximating normal for uncomplicated pregnancy. Blood chemistries reveal no striking abnormalities.

In the case of preeclampsia the total twenty-four-hour nitrogen output was 6.07 gm. The nonprotein nitrogen (which means that portion of the total nitrogen which is not precipitated by the ordinary protein precipitants) was 3.89 gm. Translated into protein equivalents the total nitrogen represents 37.9 gm. of protein, of which 24.3 gm. is nonprotein nitrogen. This individual required 61 gm. of protein to satisfy maintenance demands. She, therefore, metabolized less than half her normal requirement of protein. On admission, 64 per cent of nitrogen was in the form of nonprotein nitrogen, while the urea fraction of nonprotein nitrogen was 29 per cent. Protein loss was 13.6 gm. Under eleven days of the regime of protein stabilization the nonprotein nitrogen fraction of total nitrogen was elevated to 89 per cent, while the urea fraction of nonprotein nitrogen reached 58 per cent. Her protein loss fell to 4.12 gm. in twenty-four hours.

It is of interest to note that this patient had a digital abscess and in following her protein loss from day to day, we were unable to secure a substantial reduction in this loss until the abscess had been drained by wide incision.

In the case of eclampsia the total twenty-four-hour nitrogen on admission was 10.49 gm., or 65.25 gm. of protein. The nonprotein nitrogen fraction was 6.25 gm. of nitrogen, or 39.06 gm. of protein. Her protein loss was 26 gm. The urea fraction of nonprotein nitrogen was 42 per cent. After twenty-two days under protein stabilization the nonprotein nitrogen fraction of total nitrogen was 90 per cent, while the urea fraction was elevated 83 per cent. Protein loss at this time was 2.6 gm.

These results are offered with the hope that others may find them useful, and in using the regime contribute to a further knowledge of the fundamentals of protein metabolism in normal and complicated gestation.

18. **Theca Cell Tumors.** Dr. Samuel H. Geist, New York, N. Y.  
(For original article, see page 480, October issue.)

## DISCUSSION

DR. CAREY CULBERTSON, CHICAGO, ILL.—Last year I showed before this Society certain microphotographs and microscopic slides of ovarian tumors that were hormone producing. Among these were granulosa cell and theca cell tumors. In his presentation at this time Dr. Novak grouped together the granulosa cell and theca cell growths, on the basis that the two were of common origin. He thought it best from the clinical point of view, also for teaching purposes, to regard them as of one group. At that time I pointed out that while this made for simplification clinically, the pathologist probably would not accept a common grouping of the two tumors. We now have Dr. Geist's admirable presentation of fine specimens of theca cell tumors.

In my limited experience with these structures I have seen chiefly the granulosa cell growths but have had the privilege of studying three theca cell ones. Two of these were those already reported by Melnick and Kantor. Kantor's specimen had with it the uterus which showed a marked endometrial hyperplasia. The other tumor, Barrett's, also from the Cook County Hospital, was not accompanied by the uterus, but in both cases the patients, who were past 60 years of age, had had metrorrhagias.

The third specimen I have studied was from the Presbyterian Hospital, a case of Dr. Edward Allen's. The patient was fifty-one years of age and had bled in excess during 1922 and 1923 when she was treated by radiotherapy for what was thought to be uterine fibroids. She had not bled since and the tumor proved to be a theca-celled one.

I have recently seen in the surgical laboratory at the County Hospital a hard ovarian tumor which proved to be an ordinary adenocarcinoma. The patient from whom this tumor was taken had given a positive reaction to the Friedman test prior to operation, for which reason it had been regarded as probable that the tumor was one of these hormone producing ones. This brings up the interesting point of pre-operative hormone tests in our abdominopelvic tumors as one method of studying their characteristics.

I have a cut section of an endometrium which shows active menstrual reaction, obtained from a patient sixty-five years of age who had had her menopause fifteen years earlier. She had shown irregular bleeding, not quite as regular as three normal menstrual periods, but enough like to make her think that she was menstruating, as indeed this section shows she was. This patient was suffering from definite advanced carcinoma of the stomach, with bilateral tumors of the pelvis, the hard ovarian growth known as the Krukenberg tumor.

This brings up again the question as to whether such growths may not on occasion contain theca or granulosa cells. There is no ovarian tumor more mixed in its characteristics, in its cellular formation, and it is suggested that that portion of the tumor which is ordinarily regarded as sarcomatous may really be the granulosa or theca-celled type.

This further suggests, then, the hormonal study of all tumors of the pelvis in women. It would be well worth while to study these tumors from that point of view by preoperative physiologic examination, employing the Aschheim-Zondek or the Friedman test, as well as by the more recent "fish test" (bitterling) which seems to be a test of hormones rather than of pregnancy.

DR. EMIL NOVAK, BALTIMORE, MD.—The ideal plan for a discussion of such a subject as this would be for the group interested in gynecologic pathology to sit at microscopes and go over the specimens together. It is difficult to draw conclusions from a few slides thrown on the screen, especially when dealing with tumors

in which the examination of many slides from various parts is often essential for intelligent diagnosis.

So far as the pictures of the gross specimens are concerned, all of these tumors would seem to conform to the type of granulosa cell growth, with the possible exception of the third case, in which the tumor looks almost like a fibroma. It is not rare for granulosa cell tumors to be quite or almost solid, and to present the yellowish areas which Dr. Geist has stressed, although many, of course, present small or even very large cysts.

There is no tumor of the ovary which can assume a more varying microscopic picture than the granulosa cell cancer, as we have found in the study of more than 40 cases, and yet the diagnosis is in most cases relatively easy if one is familiar with these variations.

The chief motif of Dr. Geist's paper is the emphasis which he places upon the distinction between theca cell tumors and granulosa cell tumors, a distinction which does not seem to me justified. A study of undoubted granulosa cell tumors will often show areas exactly similar to those which have been shown on the screen as characterizing theca-cell growths. In one and the same tumor different areas may show a finely folliculoid pattern, a cylindromatous pattern, or a picture indistinguishable from sarcoma. Both granulosal and thecal cells arise from the same embryonic mesenchymal elements of the ovary, the corresponding tumors developing most often as frankly granulosal tumors, occasionally as theca cells tumors, often as intergrades or interminglings of the two types. I can see no good reason for designating the theca cell variety as a separate entity, any more than, for example, selecting the cylindroma for separate classification.

In laying such stress upon the nature and distribution of the lipoidal content of these tumors, Dr. Geist has emphasized what I think is a very unsubstantial criterion. One must remember that we are dealing with tumor cells of an embryonic rather than an adult type, and that the lipoidal content may thus undergo much modification, even if, as I do not believe is true, the lipoidal differences of the adult cells were established beyond question. To make what I think is a fair comparison, the normal squamous epithelium of the pars vaginalis is rich in glycogen, as shown by the Schiller technic. The cells of the cancer originating in this same epithelium, however, are lacking in glycogen. Again, there is a marked difference as regards lipoids in one and the same corpus luteum before and after menstruation.

The mere finding of estrin likewise is of no especial significance, as this substance is found in many body tissues, and, of course, in granulosa cell tumors. More important would be the study of the endometrium, and I wonder whether this was available in the third case, which grossly suggested the granulosa cell tumor less than any of the others.

My own reaction to the available evidence is that theca cell tumors are not to be considered a separate entity, but as simply a subdivision of the large group commonly included under the designation of granulosa cell tumors. A better name for the whole group would probably be progranulosa cell carcinoma.

DR. GEIST (Closing).—I cannot quite agree with Dr. Novak that the theca cell tumor is really a granulosa cell neoplasm. Given two types of cells the probabilities are that if these cells are capable of producing tumors we should have two types of tumors, and if this is so we should attempt to identify them as independent types. Dr. Novak spoke of the protean nature of these granulosa cell tumors—perhaps other tumor types are being classified in this granulosa cell group that really do not belong there.



I believe that there is a distinct difference between the granulosa cell tumor and the type I have demonstrated this morning. In none of the neoplasms termed theca cell tumors did careful histologic search reveal any areas typical of granulosa cell growths. The lipid type and distribution I believe is important. The difference in distribution is very characteristic as has been mentioned by Schiller and demonstrated by me. The difference in type is also important. The main mass of lipid in the granulosa cell tumor is phospholipoid; the main mass in the thecal tumor is cholesterol or cholesterol-ester.

Another point of differentiation is that the theca tumors are benign, while the granulosa cell tumor in many reported instances is definitely malignant.

In the second case the patient had a marked enlargement of her breast and profuse and irregular menstrual periods. The breast receded after removal of the tumor and the menstrual periods became absolutely normal, suggesting a hormonal influence. In the third case we did not get a specimen of the mucosa.

I do not think our criteria are sufficiently precise at the present time but I do believe that with more careful study we will be able to distinguish between these different tumor types. It may prove of some practical value to the surgeon when he opens the abdomen.

**19. Experience With Multiple Dose Roentgen Therapy in Malignant Diseases of the Uterus and Ovaries.** Dr. William P. Healy, New York, N. Y. (For original article, see page 613, November issue.)

#### DISCUSSION

DR. LEWIS C. SCHEFFEY, PHILADELPHIA, PA. (By invitation.)—I shall discuss the treatment of a series of cases of carcinoma of the cervix and the results obtained on the Gynecologic Ward Service at Jefferson Medical College Hospital, Philadelphia.

From 1921 until 1930, 155 patients were observed; of these 145 were treated, of which group over 95 per cent have been definitely followed up. The few untraced patients are, of course, regarded as dead. Too much emphasis cannot be placed on the desirability of a well-organized follow-up clinic, personally supervised by those administering the treatment.

Based on the Schmitz classification, in only 11.6 per cent of the patients seen has the carcinoma been thought to be limited to the cervix.

Of the 155 patients observed, in the period mentioned, 29 are alive from five to twelve years, 18.7 per cent absolute. Considering those patients treated (145) the percentage alive amounts to 20, while in addition 7 patients survived for six to eight years after their initial treatment, increasing the five-year salvage to 24.8 per cent. One patient died as an immediate result of treatment, a mortality of 0.068 per cent.

When the result of treatment of our early cases, Class I and II, is considered, 18 were observed and treated of whom 7 are alive five to twelve years, 38.8 per cent, while three patients survived from six to eight years after treatment, making the five-year salvage 55.5 per cent.

A word as to treatment: 80 per cent (118 patients) received radium applications only; 19 received x-ray subsequently; 3 were treated solely with the x-ray, while in only 5 patients was panhysterectomy resorted to, with adjuvant radiation, either as a preliminary or postoperative measure or both. Analysis of this phase of our report is enlightening but time does not permit a detailed discussion.

As noted, x-ray therapy was employed infrequently in this series, for in the earlier days its use discouraged us in certain instances, possibly because a massive dose technic, completed in three or four days, was used.

More recently we have been utilizing the multiple dose method, similar in principle to that recommended by Dr. Healy, both prior to and following the use of radium. Evaluation of this altered technic is obviously impossible as yet, but we feel that the results just tabulated will be a valuable control for future comparisons as to the efficacy of the present plan.

DR. NELSON B. SACKETT, NEW YORK CITY (By invitation).—The results from the Woman's Hospital are roughly the same as those reported by Mr. Bonney, namely: of unselected patients 1 out of 4 may be expected to survive five years or more; and 1 out of 6, about 18 per cent, may be expected to survive ten years or more. These results can be roughly doubled in the Schmitz Class I and II cases, indicating that we may hope for marked improvement by cancer propaganda resulting in early detection of cases.

That that propaganda has so far been disappointing is indicated by our experience at the Woman's Hospital, for in the first eight years of radium treatment the percentage of Schmitz Class I and II cases was roughly 21 and a fraction, whereas in the past seven years it is even lower, 18 per cent.

While we cannot estimate the results of adjuvant roentgen therapy until about 1938, since it was not given in satisfactory doses until 1933, our five-year survival rate can be expected to improve possibly 5 or 6 per cent, judging from the improvement obtained by Regaud in Paris. At the same time the total salvage by radiation therapy is not likely to be more than 35 per cent by any of those methods. Therefore it would seem that we must fall back upon prophylaxis as emphasized by Dr. Barrett at the American Medical Association last year and as formerly emphasized by the reports from Graves's Clinic.

While we talk about the salvage of life, we must remember that the patient's health after treatment is equally important or more important to herself and to her family. I think similar studies should be submitted on patients surgically treated and untreated, so that we may properly estimate whether it is worth while to give a woman with cancer of the cervix irradiation. Except for hemorrhage, which is part and parcel of cancer of the cervix, none of the complications referred to occurred in as many as 10 per cent. Roughly one-third of the pyometra cases had this complication on admission. While there are almost 10 per cent of bladder and urethral complications, many of those are very trivial and transient.

If we confine ourselves to the late bladder reaction, the figure is near 3 per cent, or comparable to that reported by Dr. Dean from the Memorial Hospital.

If we are going to differentiate the effect of the radiation from the effect of the disease itself, we should take the whole series of patients and compare them with those patients who are destined to survive.

I have tabled the percentages of complications in 638 cases at the Woman's Hospital in patients who have survived five years. There were 127 five-year cases which had complications and, with two exceptions, they are all less in the group of patients destined to survive irradiation than in the whole group, three-fourths of whom are destined to die of the disease itself. In the ten-year series the same is true.

The minus marks bring out that these figures are in every case much less than the percentages figured on patients who die of cancer, and still far less than patients untreated. A notable exception is lymphatic obstruction. Patients with varicose veins and ulcers and marked edema seem to be more frequent among the five-year survivors than in the total group; and therefore the irradiation effect

would seem to be implicated. Likewise they occur over twice as frequently in the group that has survived ten years or more. Further, in most of these patients the symptoms are transient and can be cured by elevation, massage, etc., indicating that they are effects of radiation and not of the cancer.

From the study of these complications it seemed to us that the complications came more frequently in untreated, hopeless cases, that they were less frequent in patients destined to survive than in the entire series, and that except for hemorrhage each complication occurs in less than 10 per cent of all patients treated; also that complications most often appear within a few weeks or months of death from metastases and that their appearance is of unfavorable prognostic import. Carcinoma of the stump occurred in 7 per cent of our series, and the incidence of fistula in stump cases was 12 per cent or one and one-half times the general fistula incidence.

DR. NORMAN F. MILLER, ANN ARBOR, MICH.—When such potent therapy is extended as Dr. Healy has advocated and used to full capacity, additional hazards to the patient may be expected. In a review of our own group treated very similarly to the method described we found nine patients with a fracture of the neck of the femur. Two of these showed obvious x-ray evidence of metastases. In seven there was no x-ray evidence of metastatic growth. One patient has been observed for a period of sixteen months without x-ray evidence of neoplastic involvement in the fractured hip. Two were quite ill with this hip involvement but are now able to walk. We cannot be dogmatic but the question as to whether therapy produces a trophic change (osteoporosis) must be seriously considered. The blood supply to the neck of the femur, through the ligamentum teres, is not beyond injury from the intensive remedial measures used in the treatment of cervical cancer.

DR. WALTER T. DANNREUTHER, NEW YORK CITY.—Dr. Healy has sharply differentiated between the massive unit dose and the cumulative dose of roentgen ray therapy. I have used the latter method for the past year and one-half in the treatment of carcinoma of the cervix, but up to the present time the roentgen ray therapy has been applied after the radium applications. It is quite evident from Dr. Healy's enlightening presentation that I have made a mistake by starting the cumulative x-ray immediately after the radium therapy.

Two things have impressed me in contrasting the modified Coutard method with the one previously employed; when the massive unit doses were given, using four portals of entry, the patients suffered a great deal from nausea and temporary prostration, although if they were in reasonably good condition the unpleasant symptoms soon disappeared. On the other hand, the patients treated with cumulative doses have been distressed by severe proctitis, diarrhea, intestinal hemorrhage, and discomfort in the descending colon. The likelihood of intestinal disturbance and skin destruction, stressed by Dr. Healy, cannot be too strongly emphasized. I have had a rather discouraging experience in several cases particularly, in which there was not only intense tenesmus in the colon, but also profuse bleeding.

The second thing that is striking about the cumulative dosage is that the prostration is greatly prolonged.

I recently had a patient who was subjected to the Wertheim operation, which was promptly followed by roentgen ray therapy, given daily for thirty days. Dr. Miller's suggestion that osteoporosis or osteosclerosis may result from cumulative doses is very illuminating because this patient was found to have a pathologic fracture of the neck of the right femur, without a fall or any noticeable strain of the joint. Repeated monthly x-ray pictures have shown nothing but a definite loss

of calcium in the bone. (In June, 1935, this patient sustained a pathologic fracture of the neck of the other femur, again without forcible trauma or evidence of metastasis.)

DR. KARL H. MARTZLOFF, PORTLAND, ORE.—Since a modified adaptation of the Coutard technic is probably coming into more or less general use it seems to me that we are going to see, in addition to what Dr. Miller has described, another type of late complication which will give us occasion for serious thought. Dr. Healy, I believe, just as Dr. Coutard, aims to produce an area of definite superficial skin necrosis in order that he may know that a dosage of maximum tolerance has been given. This has been termed radioepidermitis or epithelitis. I do not believe this skin change, although it appears superficial, is altogether innocuous, for it indicates that underlying vasculocconnective tissue changes are also in progress with varying degrees of endarteritis. In some individuals these changes probably are slowly progressive for years so that a patient may develop a large area of necrosis of skin and subcutaneous tissue three or four years after completion of radiation therapy. Now it is this and allied complications which the Coutard method aims to avoid by the protracted use of small daily doses of roentgen ray. The long-drawn-out period of treatment varying from forty to seventy days is one of the immediate disadvantageous aspects of Coutard's method and will probably lead to modifications whose actual effects, harmful and otherwise, may not be appreciated for several years. Therefore, I am afraid we shall see more of those cases as time goes on and I would like to ask Dr. Healy what his experience has been with this complication. Also, does he think that the unmodified employment of the Coutard procedure will actually obviate such complications?

DR. HEALY (Closing).—Dr. Dannreuther and Dr. Miller brought out the facts referred to in this paper, the great danger and the ultimate damage that may result from heavy intensive irradiation of normal tissues. I have been using roentgen ray therapy at the Memorial Hospital for fourteen years as a routine procedure and it has been a fairly constant observation in my private patients, whom I see and study closely, that in the second year following treatment in a fairly large number of the cases there will be a small area, the size of the palm of one's hand, on one or the other side in which telangiectatic changes will be observable in the skin and a brawny subcutaneous area in the fat. Why in that one area? Why not in other areas which have received the same amount of radiation? Last year I published a paper on the roentgen and radium complications. I have done six or seven eeliotomies with bowel resection for radiation damage to the intestine, the condition coming on a year or a year and a half after radiation with radium and roentgen ray as we were then using it. Now we are trying to increase the dose but you must select your cases. You cannot take a debilitated person and give her this kind of treatment, and it places upon the gynecologist and the roentgenologist a big responsibility to keep their patients under close observation during the course of treatment. I do not know how much more we shall have in the way of serious complications in two to five years after this form of therapy than we have previously had. It is probable that we will have a few more bladder lesions. Undoubtedly we will have some intestinal complications that may result in gangrene and require a resection, but if we do not have too many and if we can improve our percentage of end-results it may be worth while; or it may be that when we have finished all this effort we will find that we have about reached our maximum and cannot do more with combined roentgen and radium radiation than with radium alone. Dr. Coutard has done better and he is the only one who has developed this plan of treatment.

## WASHINGTON GYNECOLOGICAL SOCIETY

MEETING OF NOVEMBER 24, 1934

The following papers were presented:

Embryonal Cysts of the Cervix and Their Etiology, With a Report of Two Cases. Dr. J. Kotz. (For original article, see page 854.)

A Case of Bicornate Uterus With Double Cervix and Vagina, Premature Separation of the Placenta, Excision of Vaginal and Cervical Septa Followed by Delivery of a Living Child. Dr. A. E. Pagan.

Fibroids Complicated by Pregnancy: Aschheim-Zondek Reaction: Hysterectomy. Dr. H. P. Ramsey.

---

### Item

#### An Enlarged Journal

The constantly increasing demands for space in the JOURNAL make it necessary to provide an additional number of pages. Beginning with the January issue, a total of about 200 pages will be added to each volume, or approximately 400 each year. This increase in size will avoid some of the previously unavoidable delays in the publication of accepted papers and permit the expansion of certain departments, including those devoted to reviews, abstracts, and "maternal welfare." The publication of the discussions of papers read at the meetings of societies of which the JOURNAL is the official organ will also be resumed so far as this is practical. It is hoped by these additions to provide for more adequate and prompt appearance of the contributions of American authors in the special field represented by the JOURNAL and thus add to its value for those who have supported the publication by their subscriptions. A more detailed announcement of policies will appear in the January issue.

*The Editors.*

# Department of Reviews and Abstracts

---

CONDUCTED BY HUGO EHRENFEST, M.D.

---

## Selected Abstracts

### Organotherapy

Dodds, E. C.: Oestrus-Producing Hormones, Brit. M. J. 2: 1187, 1934.

Three estrus-producing hormones have been identified in the urine of pregnant women. They belong to the group of sterols, and have in common a partially hydrogenated phenanthrene ring.

The type of estrin in the circulating blood, the ovary or the placenta is unknown. Plants contain an estrus-producing substance, of same structure as estrin, named tokokinin. Vitamin D in very large doses produces estrus. Estrus-producing hormones are found linked closely with carcinogenic substances, and with vitamins and plant sterols.

Kaufmann's demonstration that menstruation can be produced in ovariectomized women by administering sufficient estrus-producing hormone and corpus luteum hormone was confirmed by the author. The former also showed that *large* doses of the hormones can produce pathologic conditions of the endometrium, i.e., cystic hyperplasia. This points to a therapeutic value in these hormones and opens a practical application for them in many gynecologic conditions hitherto treated by surgery only.

F. L. ADAIR AND S. A. PEARL.

Buschbeck: Progress in Gynecologic Hormone Therapy, Monatschr. f. Geburtsh. u. Gynäk. 98: 123, 1934.

The basis of modern hormone therapy lies in the present knowledge of the "normal dosages" which in the Women's Clinics of Berlin and Wuerzburg have been established on female castrates. A true menstrual flow is obtained with not less than 200,000 to 300,000 M.U. of follicle hormone (progynon B) and 100 clinical units of corpus luteum hormone (proluton). The writer reports 36 successes on castrated women with these doses. No failure. The corpus luteum hormone must be injected within eight days after the last progynon injection. Between 20,000 and 50,000 M.U. of progynon must be administered during the first half of the cycle.

With progynon alone in 24 cases of secondary amenorrhea menstruation-like flows were obtained, which in four cases by enretage were shown to be not true menstruations.

In a sterile woman, amenorrheic for two years, two series of injections of 100,000 units of progynon led to one flow each time and then were followed by a pregnancy.

It is impossible to say whether the therapy improved possibility of nidation or resulted in expulsion of a mature ovum. This one experience could encourage such therapy for certain cases of sterility.

In one case each of very severe pruritus and kraurosis vulva one menstruation-like flow (in climacterium) each followed the injection of 1,100,000 M.U. of progynon B.

HUGO EHRENFEST.

**Loeser, Alfred:** Artificial Production of Menstruation with Ovarian Hormones in Cases of Primary and Secondary Amenorrhoea, *J. Obst. & Gynec. Brit. Emp.* 41: 86, 1934.

The author has succeeded in producing normal menstruation in three out of five women with primary amenorrhea by giving 300,000 mouse units of a preparation of follicular hormone followed by injections of a corpus luteum hormone. The women, aged twenty-five, thirty, and thirty-eight, had never before had any genital bleeding. In each case the uterus, which was small and atrophic, increased to 5 to 7 cm. in length. The treatment was as follows: first day, 100,000 M.U.; seventh day, 100,000 M.U.; fourteenth day, 50,000 M.U.; nineteenth day, 50,000 M.U., of the follicular hormone. From the twenty-second to the twenty-sixth day inclusive, 10 rabbit units each day of corpus luteum hormone was given. Unfortunately, women subjected to this treatment menstruate only once. In general a treatment for months is necessary to produce the bleeding repeatedly at the term desired.

WILLIAM F. MENGERT.

**Buschbeck, H.:** Progress in Gynecological Hormone Therapy, *Monatsschr. f. Geburtsh. u. Gynäk.* 98: 344, 1935.

It has been shown that in completely castrated women a true menstrual flow can be effected by administering first follicular and then corpus luteum hormone. The same treatment may be used in women who have amenorrhea. The author has produced fifty menstrual periods and has thus far not encountered a single failure. He insists that large doses of both substances must be used and that the corpus luteum hormone must be given not later than eight days after the last injection of follicle hormone. The intensity of the bleeding depends upon the amount of follicle hormone and not upon the corpus luteum hormone. This information is utilized by giving women who have slight menstrual bleeding, large doses of follicle fluid during the first half of the menstrual cycle.

The results with this form of hormone treatment of dysmenorrhea are striking. The author has seen patients relieved of their pain after one injection. He has improved the regularity of menstrual cycles in women whose menses are too infrequent by the injection of follicle hormone. He has likewise obtained excellent results in cases of secondary amenorrhea, and points out that he has observed good results with follicle fluid alone. However, curettement in such cases failed to show the typical premenstrual growth of the endometrium. Hence, these bleedings are not true menstruation.

J. P. GREENHILL.

**Murphy, Douglas P.; Shoemaker, Rosemary; and Rea, Marion:** Menstrual Response to Luteinizing Extract of Pregnant Urine, *Endocrinology* 18: 203, 1934.

Luteinizing extracts of pregnancy urine injected hypodermically in five normal women, over a ten-day period beginning with the first day of the menstrual flow, was followed by no significant alteration in either subjective symptoms or blood

flow during the coexisting or two subsequent menstruations. Of five women similarly treated except that the injections were administered on a day midway between the two menses, three experienced entirely new symptoms of a painful nature, and one other subject had an eight-day period of spotting at the end of a normal three- to four-day menstrual flow.

J. THORNWELL WITHERSPOON.

**Brochier, A.:** The Use of Follicular Hormone in Premature Infants, *Bull. Soc. d'obst et de gynéc.* 23: 542, 1934.

Brochier systematically employed folliculin in doses of 1,000 International units in premature infants. Not one of the children so treated died, whereas premature infants of about the same weight and development and born under the same conditions had a high incidence of death. A remarkable fact was that the infants treated with folliculin lost only a small amount of weight and began to gain after the second day. On the other hand, the untreated babies lost a great deal of weight and did not begin to gain until after the third day.

J. P. GREENHILL.

**Macchiarulo, O.:** The Influence of Ovarian Preparations Upon the General Development of Fetuses at Term, *Folia gynae.* 31: 1, 1934.

The author found that folliculin administered to a group of pregnant guinea pigs brought about a healthier and better developed litter. The experiment was undertaken following Schiller's work on the beneficial effects of folliculin on premature infants.

MARIO A. CASTALLO.

**Sure, J. H.:** Endocrine Headaches, *Wisconsin M. J.* 33: 671, 1934.

The type of endocrine headaches varies. They may be periodical, that is, pre- or postmenstrual, and are only occasionally continual. They may be hemicranial, temporal, parietal, or occipital. They may be sufficient to incapacitate the patient, or may only be annoying. It is described as compressing or expanding. The author offers the following classification as a cause for the headache: (1) Hypergonadism, (a) hyperestrinemia, (b) hyperprolanemia A; (2) hypogonadism, (a) hypoestrinemia, (b) hypoprolanemia A; (3) hyper- and hypolutemia; (4) hyper- and hypoprolanemia B; (5) hypo- and hyperthyroidism; (6) hyper- and hypopituitarism; (7) hyper- and hypoadrenalism.

J. THORNWELL WITHERSPOON.

**Skipp, W. M.:** Pituitary Headache, *Endocrinology* 18: 596, 1934.

Eleven patients suffering from pituitary headache (10 females and 1 male) were treated with posterior pituitary extract by mouth and subcutaneously, with disappearance of the headaches. Posterior lobe extract in tablet form was given orally and infundin hypodermically. The case histories of three of the patients are given in detail. Extracts of the anterior lobe were apparently without benefit.

J. THORNWELL WITHERSPOON.

**Borovskaja, V. A.:** Clinical Observation on Hypophysectomized Patients, *Vestnik Endocrinologii (Moscow)* 4: 374, 1934.

The author studying hypophysectomized patients found in all cases without exception extreme psychical slothfulness, somnolence, increasing corpulency, motor slow-



ness, and sharp decline of sexual sensitiveness. Return of vision is usually slight, in some cases vision was not restored. Headaches in the majority of cases became noticeably lessened. These complications were treated with hypophyseal hormones, or continuous injections of Gravidan (sterile urine from six to eight weeks' pregnancy), or by repeated implantations of the pituitary gland. The author doubts the necessity of hypophysectomy, except in suspected malignancy of the pituitary gland, because this operation leads to new forms of diseases.

ALEXANDER GABRIELIANZ.

Stern, D. M.: The Zondek-Aschheim Test After Partial Hypophysectomy, Proc. Roy. Soc. Med. London 27: 1501, 1934.

In July, 1931, the then twenty-one-year-old patient was admitted for signs of acromegaly, bitemporal hemianopia of scotomatous type. Skiagram showed enlarged sella turcica. A few days later a large part of the anterior pituitary body was extirpated, an adenomatous growth.

A year later she married, and in September, 1932, realized that she was pregnant. The Aschheim-Zondek reaction was found positive. She passed through a normal pregnancy and was delivered in January, 1933, of a 7½-pound normal baby.

The concentration of gonadotropic hormones was definitely below normal. The reaction was negative six weeks postpartum.

It remains an open question whether these hormones were derived from the small fragment of remaining anterior pituitary body or had some other source, such as embryonic trophoblast.

HUGO EHRENFEST.

Arapoff, D. A.: Homotransplantation, as a Method of Treatment of Endocrinopathies, Vestnik Endocrinologii (Moskow) 4: 439, 1934.

In the treatment of certain endocrinopathies (such as cretinism, eunuchoidism, sexual impotence in men, hypofunction of the ovary), the author, in 67 cases, used transplantations of thyroid gland, testicle and ovaries from human beings who had died from accidents. Glands were taken from the corpse one to six hours after death, were preserved in physiologic saline solution and kept on ice, until the results from Wassermann reaction were known. Glands were implanted in subcutaneous tissue of abdomen or breast. In fifteen cases of transplantation of testicle the method of Voronoff was used. Permission for performing the autopsy for the removal of required glands was granted by the Prosecuting Attorney in 1931.

For transplantation of the hypophysis the gland of calf embryo, monkey, sheep, pig, and goat was used. The human hypophysis was difficult to remove. The most favorable results were obtained with thyroid gland implants.

ALEXANDER GABRIELIANZ.

Allen, E., Gardner, W. V., and Diddle, A. W.: Experiments with Theelin and Galactin on Growth and Function of the Mammary Glands of the Monkey, Endocrinology 19: 305, 1935.

Ten Macacus monkeys weighing from 3,365 to 6,050 gm. and at various stages of sexual maturity were injected with galactin, or prolactin, with or without previous theelin treatment. Lactation was induced in four mature animals and in one animal just reaching sexual maturity, following the injections of six to nine rabbit units of galactin or prolactin. Three of the mature animals possessed one

or both ovaries; the other two were ovariectomized. The two ovariectomized animals had been previously injected with 2,150 and 1,700 R.U. of theelin. Treatment with galactin was begun in three of the above normal animals on the third, fifteenth, and twentieth days, respectively, of the menstrual cycle.

The lactation-stimulating hormone in doses from 3 to 13 rabbit units did not induce lactation in the remaining 5 animals, 3 of which were just reaching maturity and 2 of which were immature. From 1,300 to 1,700 R.U. of theelin were injected in all cases before beginning galactin treatment.

All of the monkeys with mature mammary glands responded positively to galactin in the doses and over the interval given. Partially developed mammary glands of younger monkeys did not respond.

J. THORNWELL WITHERSPOON.

Kabak, A. M., and Kizelshtein, M. S.: *Endocrine Factors of Lactation*, *Vestnik Endocrinologii* (Moscow) 4: 460, 1934.

The authors analyze the results of the injections of different hormones in 60 sheep. Another fifteen sheep were taken as control. (1) The urine from women in the middle of pregnancy was injected daily into the sheep during fifteen consecutive days (from 10 c.c. to 22 c.c. daily). The lactation was suppressed. (2) The alkaline extract of the hypophysis injected the same length of time, 22 c.c. daily, did not give changes in the quantity of milk. Smaller doses (5 c.c.) gave an increase in milk only during the experiment. (3) Prolan at the time of the experiment suppressed lactation, but when three injections (300 M.U. daily) were given a notable rise in the lactation curve occurred, surpassing the control sheep in the long period of observation (twenty-two days).

ALEXANDER GABRIELIANZ.

Jeffcoate, T. N. A.: *Sterility Due to Ovarian Dysfunction*, *Brit. M. J.* 1: 345, 1935.

The author presents the view that sterility, in patients with no menstrual upset and no abnormalities of organs, is due to the absence of ovulation. Anovular menstruation is frequent. It is a serious factor in sterility. It accounts for the majority of cases in which menstrual upset is an additional symptom. It is responsible for unsuccessful results in the treatment of some obvious lesions, anteversion or retroversion. Failure of follicular rupture explains the physiologic sterility in early life and late middle ages. Anovular menstruation is most frequent at these periods. Sterility associated with neoplasms is not the result of these tumors: both conditions are manifestations of a primary ovarian disorder.

F. L. ADAIR AND S. A. PEARL.

Hamblen, E. C.: *Results of Preoperative Administration of an Extract of Pregnancy Urine: A Study of the Ovaries and of the Endometria in Hyperplasia of the Endometrium Following Such Administration*, *Endocrinology* 19: 169, 1935.

A study of the ovaries and of the endometria of eleven patients with hyperplasia of the endometrium following injections of an APL extract is presented. Single injections ranged from 100 to 400 R.U.; the frequency of administration varied from one to four times daily, while the duration of treatment was from four to nine days and the total dosage from 2,400 to 8,200 R.U. Patients with gross inflammatory changes or with benign or malignant tumors of the generative tract were not studied. Endometrial specimens were obtained before administration of the extract and after its injection, with corresponding ovarian specimens.

These experiments showed that APL extract does not affect primordial or early follicles and that it acts primarily upon maturing or mature ones, increasing the degenerative changes commonly observed and probably producing cystic degeneration. In a mature group of patients with hyperplasia, however, APL extract apparently produced recent corpora lutea. This observation was not noted in an immature group of patients, also exhibiting hyperplasia of the endometrium. Hemorrhage into or about follicles was considered an unimportant finding, while endometrial changes were produced in only one instance.

J. THORNWELL WITHERSPOON.

**Cornil, L., and Escarras, A.: Experimental Researches on the Gonadotropic Hormone in Uterine Epithelioma, *Endocrinol. e patol. costit.* 3: 208, 1934.**

In twenty-five cases of cervical epithelioma the authors found the Friedman test positive in thirteen cases; of these, ten were of the predominating basal cell type. The test was doubtful seven times of which four cases were of the predominating spindle cell type. It was negative five times; four cases were of the spindle cell type. In ten cases of extragenital epithelioma (eight in women and two in men) there was only one doubtful positive Friedman test; the remaining nine gave a negative test.

MARIO A. CASTALLO.

**Umezawa, R.: Melanocyte Reaction of Preparations of the Pituitary Body and the Urine of Cancer Patients, *Jap. J. Obst. & Gynee.* 18: 2, 1934.**

Umezawa found that he could produce a strongly positive melanocyte reaction not only by the injection of preparations of the posterior pituitary lobe, but also by the administration of anterior lobe preparations, and the so-called anterior pituitary hormones. He found that cancer patients excrete the melanocyte hormone in their urine. Judging from this occurrence the author believes that cancer and pituitary secretions have an intimate relationship. Since he noticed that a positive melanocyte reaction can be found only in the urine of cancer patients, he believes that this reaction can be employed for the immediate diagnosis of cancer.

J. P. GREENHILL.

**Magistris, H.: Antihormonal Sterilization of Female Animals. (1) By Preparations from Male Sexual Glands, *Rev. Soc. Argent. de biol.* 10: 179, 1934.**

The author prepared testicular substance according to the method of Neumann. He injected various amounts of this preparation into female white mice and obtained temporary sterilization of the animals. The smaller amounts, using two to four testicles of male white mice, did not produce sterilization in the female. Large amounts, twelve to fourteen testicles, in some cases caused death. A medium amount, eight to twelve testicles in solution, gave the best results.

MARIO A. CASTALLO.

# INDEX TO VOLUME 30

## AUTHORS INDEX\*

### A

- ADAIR, FRED L., American committee on maternal welfare, 868
- , DAVIS, M. EDWARD, KHARASCH, M. S., AND LEGAULT, ROMEO R., A study of a new and potent ergot derivative, ergotocin, 466
- ALDRIDGE, ALBERT H., AND WATSON, PAUL, Analysis of end-results of labor in primiparas after spontaneous versus prophylactic methods of delivery, 554
- ALLEN, EDWARD D., (WITH THOMAS, WILLIAM A., BAUER, CARL P., AND FREELAND, M. R.), Toxemias of late pregnancy, 665
- , JENSEN, LLOYD B., AND WOOD, I. H., Clinical and bacteriologic observations in trichomonas vaginitis, 565
- ALLEN, WILLARD M., AND REYNOLDS, SAMUEL R. M., Physiology of corpus luteum, 309
- ANDERSON, JAMES F., (WITH HANLEY, BERNARD J.), A review of 190 cases of heart disease complicating pregnancy, 243
- ANSPACH, BROOKE M., Contributions of Great Britain to gynecology and obstetrics, 459
- AUER, EUGENE S., Cancer of female urethra, 318

### B

- BAKER, R. D., (WITH HAMBLEN, E. C., AND MARTIN, D. S.), Blastomycosis of female reproductive tract, 345
- BALASQUIDE, L. A., Case of chondrodysplasia with delivery by cesarean section, 430
- BARTHOLOMEW, R. A., Control of restlessness in painless labor, 866
- BAUER, CARL P., (WITH THOMAS, WILLIAM A., ALLEN, EDWARD D., AND FREELAND, M. R.), Toxemias of late pregnancy, 665
- BONNEY, VICTOR, Treatment of carcinoma of cervix by Wertheim's operation, 815
- BOWERS, A. TALBERT, Cesarean section: factors influencing mortality, 193
- BOYD, ELDON M., Blood lipids in eclampsia, 323
- BRACK, C. BERNARD, (WITH HUNDLEY, J. MASON, JR., WALTON, HENRY J., HIBBITS, JOHN T., AND SIEGEL, ISADORE A.), Physiologic changes occurring in urinary tract during pregnancy, 625
- BRADY, LEO, Cancer of cervix and vagina in a case of complete procidentia, 277
- BRAWNER, JAMES N., JR., (WITH TELINDE, RICHARD W.), Experiences with amniotin in treatment of gonococcal vaginitis in children, 512
- BREWER, JOHN L., (WITH FITZGERALD, JAMES E.), Extrauterine pregnancy, 264

- BROWN, T. K., AND KLEINE, H. L., Use of dilaudid in gynecologic surgery, 89
- BRYANT, RICHARD D., Veratrum viride in treatment of eclampsia, 46

### C

- CALDWELL, W. C., MOLOY, H. C., AND D'ESOP, D. ANTHONY, Further studies on mechanism of labor, 763
- CANNELL, DOUGLAS, AND DOUGLASS, MARION, Complications following cauterization of cervix uteri, 376
- CARRELL, WILLIAM D., Intrauterine gas gangrene with recovery, 858
- CASTALLO, MARIO A., AND MONTGOMERY, THADDEUS L., Management of prenatal and postnatal cervix, 37
- CHEATHAM, GOODE R., AND PECK, ABEL E., Injection of varicose veins during pregnancy, 392
- COLLINS, C. G., (WITH TYRONE, C. H., AND ROMANO, S. A.), Tubal gestation, 112
- COLLINS, DONALD C., (WITH COUNSELLER, VIRGIL S.), Fibromyoma of cervix uteri, 108
- , (WITH COUNSELLER, VIRGIL S.), Tuberculosis of cervix uteri, 830
- COUNSELLER, VIRGIL S., AND COLLINS, DONALD C., Fibromyoma of cervix uteri, 108
- , AND —, Tuberculosis of cervix uteri, 830
- CROTTY, JOSEPH G., Fetus papyraceous in twin pregnancy, 296
- , Occiput posterior, 97
- CUMMINGS, W. G., (WITH LASH, A. F.), Porro cesarean section, 199
- CUTLER, ORAN I., Corpus luteum tumor, 131

### D

- DAICHMAN, ISIDORE, AND KORNFIELD, GEORGE, Pregnancy complicating cardiac disease, 386
- DAILY, EDWIN F., Cesarean section, 204
- , (WITH DIECKMANN, WILLIAM J.), Blood loss during cesarean section, 221
- , (WITH DIECKMANN, WILLIAM J.), Role of blood transfusion in treatment of obstetric hemorrhage, 1
- DANNREUTHER, WALTER T., Primary carcinoma of fallopian tube, 724
- DAVIS, CARL HENRY, Hypothyroidism as a problem in women, 570
- DAVIS, M. EDWARD, (WITH ADAIR, FRED L., KHARASCH, M. S., AND LEGAULT, ROMEO R.), Study of new and potent ergot derivative, ergotocin, 466
- DERBRUCKE, M. G., An instance of like monsters in successive pregnancies, 429
- D'ESOP, D. ANTHONY, (WITH CALDWELL, W. C., AND MOLOY, H. C.), Further studies on mechanism of labor, 763

\*July, pp. 1-155; August, pp. 159-308; September, pp. 309-458; October, pp. 459-608; November, pp. 609-762; December, pp. 763-928.

- DIECKMANN, WILLIAM J., AND DAILY, EDWIN F., Blood loss during cesarean section, 221
- , AND —, Rôle of blood transfusion in treatment of obstetric hemorrhage, 1
- DIETHELM, MARTIN W., AND RAMSEY, THOMAS L., Tuberculous endometritis, 420
- DODDS, E. C., Relationship between estrogenic substances and cancer, 301 (Editorial)
- DOUGLAS, R. GORDON, New instrument for accurate reading of measurement of diagonal conjugate, 141
- DOUGLASS, MARION, (WITH CANNELL, DOUGLAS), Complications following cauterization of cervix uteri, 376
- DUNN, CHARLES WILLIAM, Hormonal induction of menstruation in amenorrheas of from three months' to nine years' duration, 186

## F

- FALK, HENRY C., AND NAHON, RALPH, Electrouterography, 403
- FERGUSON, JOHN A., AND OTIS, ISRAEL S., Full-term unilateral tubal twin pregnancy, 139
- FITZGERALD, JAMES E., AND BREWER, JOHN I., Extrauterine pregnancy, 264
- FLUHMAN, C. F., Ovary-stimulating factors and antihormones, 584
- FOX, PAUL C., Inversion of uterus in two successive pregnancies, 295
- FRASER, WILLIAM G., Spontaneous evolution of transverse presentation, 732
- FREELAND, M. R., (WITH THOMAS, WILLIAM A., ALLEN, EDWARD D., AND BAUER, CARL P.), Toxemias of late pregnancy, 665
- FILLERTON, WILLIAM D., Modified vaginal speculum, 297

## G

- GARDNER, GEORGE H., When is surgery indicated in retrodisplacement of uterus? 596
- GEIST, SAMUEL H., Histogenesis of certain ovarian tumors and their biologic effects, 659
- , Theca cell tumors, 489
- GOLDSTINE, MARK T., Nonpolypoid sarcoma of cervix uteri, 145
- , Sarcoma and adenocarcinoma of body of uterus; adenocarcinoma of cervix, 143
- , Squamous cell carcinoma of cervix; adenocarcinoma of fundus of uterus, 137
- GOODALL, J. R., Toxemia of pregnancy, 577
- GOULD, CHARIS, AND HIRST, B. C., Current techniques for obstetric analgesia and anesthesia, 257
- GRAD, HERMAN, Prevention of excoriation of perineum from silver wire sutures, 863
- GREEN, BRADFORD, AND MILLER, C. KENNETH, Pregnancy in a patient with complete double uterus, 281
- GUSTAFSON, G. W., Massive collapse of lung following cesarean section, 425

## H

- HAMBLEN, E. C., BAKER, R. D., AND MARTIN, D. S., Blastomycosis of female reproductive tract, 315

- HANLEY, BERNARD J., AND ANDERSON, JAMES F., Review of 190 cases of heart disease complicating pregnancy, 243
- HARDEN, BOYD, MCELLEROY, W. S., AND HUGGINS, R. R., Protein stabilization in preeclampsia and eclampsia, 524
- HARER, W. BENSON, (WITH MCGLINN, JOHN A.), Hematometra, 704
- , (WITH MCGLINN, JOHN A.), Treatment of abruptio placentae, 226
- HEALY, WILLIAM P., Experience with multiple dose roentgen therapy in malignant diseases of uterus and ovaries, 613
- HEANEY, N. SPROAT, A series of 627 vaginal hysterectomies performed for benign disease with three deaths, 269
- HERMANN, CLINTON S., (WITH SOLOFF, LOUIS A.), Chronic typhoid abscess of ovary, 290
- HIBBITTS, JOHN T., (WITH HUNDLEY, J. MASON, WALTON, HENRY J., SIEGEL, ISADORE A., AND BRACK, C. BERNARD), Physiologic changes occurring in urinary tract during pregnancy, 625
- HIRST, B. C., (WITH GOULD, CHARIS), Current techniques for obstetric analgesia and anesthesia, 257
- HOLLOWAY, HOWARD J., Ovarian pregnancy, 286
- HOLMAN, ALBERT, AND MATHIEU, ALBERT, Intravenous anesthesia with evipal soluble, 118
- HUGGINS, R. R., (WITH HARDEN, BOYD, AND MCELLEROY, W. S.), Protein stabilization in preeclampsia and eclampsia, 524
- HUNDLEY, J. MASON, JR., WALTON, HENRY J., HIBBITTS, JOHN T., SIEGEL, ISADORE A., AND BRACK, C. BERNARD, Physiologic changes occurring in urinary tract during pregnancy, 625

## I

- ISRAEL, S. LEON, Vaginal aplasia and creation of an artificial vagina, 273

## J

- JENSEN, LLOYD B., (WITH ALLEN, EDWARD, AND WOOD, I. H.), Clinical and bacteriologic observations in trichomonas vaginitis, 565

## K

- KAMINSTER, SANFORD, AND REYNOLDS, SAMUEL, R. M., Motility in transplanted, denervated uterus, 395
- KANTER, A. E., Lipoma of broad ligament, 296
- KEENE, FLOYD E., Treatment of dysmenorrhea by presacral sympathectomy, 534
- KIHARASHI, M. S., (WITH ADAIR, FRED L., DAVIS, M. EDWARD, AND LEGAULT, ROMEO R.), Study of new and potent ergot derivative, ergotoxin, 466
- KING, ARTHUR G., Determination of rupture of membranes, 860
- KLEINE, H. L., (WITH BROWN, T. K.), Use of dihydral in gynecologic surgery, 89
- KORNFELD, GEORGE, (WITH DAICHMAN, ISIDORE), Pregnancy complicating cardiac disease, 386
- KOSTER, HARRY, AND SHEINFELD, WILLIAM I., Ectopic pregnancy, 93
- KOTZ, J., Embryonal cysts of cervix and their etiology with report of two cases, 854

KRAMER, DAVID W., Some problems in pregnancy and diabetes, 68

L

LASH, A. F., Human ovum in a salpingitis isthmica nodosa, 287

—, AND CUMMINGS, W. G., Porro cesarean section, 199

LEGAULT, ROMEO R., (WITH ADAIR, FRED L., DAVIS, M. EDWARD, AND KHARASCH, M. S.), Study of a new and potent ergot derivative, ergotocin, 466

LEVENTHAL, MICHAEL L., (WITH STEIN, IRVING F.), An analysis of 381 cesarean section cases in a ten-year period at Michael Reese Hospital, 192

LITT, SOL, Tube for collection of urine under aseptic conditions, 433

—, AND STRAUSS, HERMAN A., Monoamniotic twins, one normal, the other anencephalic; multiple true knots in cords, 728

LOCKHART, HAROLD A., Cancer of uterus in childhood, 76

LULL, CLIFFORD B., Chorionepithelioma following full-term pregnancy, 730

M

MACFARLANE, CATHARINE, Factor of birth trauma in cancer of uterine cervix, 133

MARTIN, D. S., (WITH HAMBLIN, E. C., AND BAKER, R. D.), Blastomycosis of female reproductive tract, 345

MARYAN, HARRY O., New colposcope, 148

MATHIEU, ALBERT, (WITH HOLMAN, ALBERT), Intravenous anesthesia with evipal soluble, 118

MAYES, H. W., Mercurochrome to secure vaginal antiseptics during labor, 80

MAZER, CHARLES, AND SPITZ, LOUIS, JR., Therapeutic value of low-dosage irradiation of pituitary gland and ovaries in functional menstrual disorders, 214

MAZZOLA, VINCENT P., AND TORREY, MARCELS A., An experimental study of effects of intravenous injections of hypertonic glucose solution (50 per cent) on the circulation of the cat, 339

MCELLROY, W. S., (WITH HARDEN, BOYD, AND HUGGINS, R. R.), Protein stabilization in preeclampsia and eclampsia, 524

MCGLINN, JOHN A., AND HARER, W. BENSON, Hematometra, 704

—, AND —, Treatment of abruptio placenta, 226

MCMAHON, MARY A., (WITH ROWE, ALLAN WINTER, AND RILEY, GERTRUDE A.), Metabolism of levulose, 841

MEEKER, LOUISE H., (WITH MOENCH, G. H.), Diffuse sarcoma of endometrium, 135

MENDES, THOMAS O., AND MILLER, J. DEANE, Recent advances in hysterography, 590

MILLER, C. KENNETH, (WITH GREEN, BRADFORD), Pregnancy in a patient with complete double uterus, 281

MILLER, J. DEANE, (WITH MENDES, THOMAS O.), Recent advances in hysterography, 590

MILLER, NORMAN F., Treatment of vesicovaginal fistulas, 675

MOENCH, G. H., AND MEKKER, LOUISE H., Diffuse sarcoma of endometrium, 425

MOLOY, H. C., (WITH CALDWELL, W. E., AND D'ESOP, D. ANTHONY), Further studies on mechanism of labor, 763

MONTGOMERY, THADDEUS L., (WITH CASTALLO, MARIO A.), Management of prenatal and postnatal cervix, 37

N

NAHON, RALPH, (WITH FALK, HENRY C.), Electrouterography, 403

NATHANSON, JOSEPH N., A parallel study of labor in young and old primiparas, 159

NEILL, WILLIAM, JR., Pregnancy complicated by carcinoma of cervix, 414

NICHOLSON, WILLIAM R., BARTON COOKE HIRST, in memoriam, 609

NORTON, JAMES F., A review of twenty-six cases of extraperitoneal (Latzko) cesarean section, 209

NOTES, BERNARD, Routine treatment of gonorrhea in females, 121

NOVAK, EMIL, Some newer aspects of reproductive physiology, 495

NUGENT, FRED B., Primiparous perineum after forceps delivery, 249

O

OBERST, FRED W., AND WOODS, E. B., Studies in glutathione, 232

OTIS, ISRAEL S., (WITH FERGUSON, JOHN A.), Full-term unilateral tubal twin pregnancy, 139

P

PECK, ABEL E., (WITH CHEATHAM, GOODE R.), Injection of varicose veins during pregnancy, 392

PIANEUF, LOUIS E., Place of colpectomy in treatment of uterine and vaginal prolapse, 544

POMMERENKE, W. T., AND ROGERS, W. C., Sex prediction test of Dorn and Sugarman, 380

POSNER, A. CHARLES, Abdominal pregnancy with delivery of a living child, 293

—, AND PULVER, MICHAEL, An analysis of labor in young girls, 357

PULVER, MICHAEL, (WITH POSNER, A. CHARLES), An analysis of labor in young girls, 357

R

RABBINER, BENJAMIN, Torsion of pregnant uterus in patients with kyphotic pelvis, 136

RANSEY, THOMAS L., (WITH DIETHELM, MARTIN W.), Tuberculous endometritis, 420

REYCHART, JAMES L., Tribromethynol premedication in operative gynecology, 332

REYNOLDS, SAMUEL R. M., (WITH KAMINSKY, SANFORD), Motility in transplanted, denervated uterus, 395

—, (WITH ALLEN, WILLARD M.), Physiology of corpus luteum, 309

RICHARDSON, EDWARD H., Total versus subtotal abdominal hysterectomy in benign uterine disease, 237

RILEY, GERTRUDE A., (WITH ROWE, ALLAN WINTER, AND MCMAHON, MARY A.), Metabolism of levulose, 841

ROBINSON, M. R., Surgical treatment of ovarian dysfunctions, 18

ROGERS, W. C., (WITH POMMERENKE, W. T.), Sex prediction test of Dorn and Sugarman, 380

- ROMANO, S. A., (WITH TYRONE, C. H., AND COLLINS, C. G.), Tubal gestation, 112
- ROSENFELD, SAMUEL S., Treatment of persistent occipitoposterior position by 180 degree manual rotation of occiput, 364
- ROSENTHAL, ALEXANDER H., Melanoma of urethra, 115
- ROWE, ALLAN WINTER, McMANUS, MARY A., AND RILEY, GERTRUDE A., Metabolism of levulose, 841
- RUDOLPH, LOUIS, Anencephalic monster complicated by an impacted ovarian cyst, 855

## S

- SEARS, NATHAN P., Treatment of elusive ulcer of bladder by application of pure phenol, 85
- SHARP, E. A., Historical review of a syndrome embracing uteroovarian atrophy with persistent lactation, (Frommel's disease), 411
- SHEINFELD, WILLIAM I., (WITH KOSTER, HARRY), Ectopic pregnancy, 93
- SIEGEL, ISADORE A., (WITH HUNDLEY, J. MASON, JR., WALTON, HENRY J., HIBBITTS, JOHN T., AND BRACK, C. BERNARD), Physiologic changes occurring in urinary tract during pregnancy, 625
- SMITH, L. HOWARD, Bilateral peripheral paralysis of radial nerve in a newborn infant, 283
- SMITH, PHILIP HAMBLIN, Brenner tumor of ovary, 724
- , Hemorrhage in late pregnancy, 62
- SOLOFF, LOUIS A., AND HERMANN, CLINTON S., Chronic typhoid abscess of ovary, 290
- SPITZ, LOUIS, JR., (WITH MAZER, CHARLES), Therapeutic value of low-dosage irradiation of pituitary gland and ovaries in functional menstrual disorders, 214
- STEIN, IRVING F., Consideration of phenomenon of ovulation and its relation to sex cycle, 710
- , Myofibroma of ovary with heteroplastic bone formation, 289
- , AND LEVENTHAL, MICHAEL L., An analysis of 381 cesarean section cases in a ten-year period at Michael Reese Hospital, 192
- STRAUSS, HERMAN A., (WITH LITT, SOL), Monoamniotic twins, one normal, the other anencephalic, multiple true knots in cords, 728

## T

- TARNOWSKY, GEORGE DE, Tubal reimplantation—in retrospect, 696
- TEEL, HAROLD M., Study of fetal mortality in patients with organic heart disease, 53

- TELINDE, RICHARD W., AND BRAWNER, JAMES N., JR., Experiences with amniotin in treatment of gonocoeccal vaginitis in children, 512
- THOMAS, WILLIAM A., ALLEN, EDWARD D., BAUER, CARL P., AND FREELAND, M. R., Toxemias of late pregnancy, 665
- TOMPKINS, PENDLETON, Results of treatment of benign lesions of cervix uteri, 369
- TORREY, MARCUS A., (WITH MAZZOLA, VINCENT P.), An experimental study of effects of intravenous injections of hypertonic glucose solution (50 per cent) on circulation of cat, 339
- TUCK, VERNON L., Clinical test of newly recognized oxytocic principle of ergot and a new method of administration, 718
- TYRONE, C. H., ROMANO, S. A., AND COLLINS, C. G., Tubal gestation, 112

## V

- VARZHABEDIAN, MIHRAN A., Observations on normal sex ratio of albino rats and their artificial variation, 124
- VOEGELIN, ADRIAN W., Abdominal pregnancy with removal, after eighteen years, of a six months' lithopedion, 129

## W

- WALTON, HENRY J., (WITH HUNDLEY, J. MASON, JR., HIBBITTS, JOHN T., SIEGEL, ISADORE A., AND BRACK, C. BERNARD), Physiologic changes occurring in urinary tract during pregnancy, 625
- WATSON, PAUL, (WITH ALDRIDGE, ALBERT H.), Analysis of end-results of labor in primiparas after spontaneous versus prophylactic methods of delivery, 554
- WATTS, RUTH M., Effect of administration of preparations of growth hormone of anterior lobe of pituitary upon gestation and weight of newborn (albino rats), 174
- WEINSTEIN, MANDEL, Ruptured interstitial pregnancy, 849
- WEITZNER, SAMUEL F., Simple roentgenographic method for accurately determining true conjugate diameter of pelvis, 126
- WOOD, I. H., (WITH ALLEN, EDWARD, AND JENSEN, LLOYD B.), Clinical and bacteriologic observations in trichomonas vaginitis, 565
- WOODS, E. B., (WITH OBERST, FRED W.), Studies in glutathione, 232

## Y

- YELLEN, HIRAM S., Bloodless circumcision of newborn, 146

# SUBJECT INDEX\*

## A

- Abdominal and pelvic regions, practical surgery of, (Kennedy), 752 (Book review)
- hysterectomy in benign uterine disease, total versus subtotal, (Richardson), 237
- pregnancy with delivery of a living child, (Posner), 293
- with removal, after eighteen years, of a six months' lithopedion, (Voegelin), 129
- Abruptio placentae, treatment of, (McGinn and Haver), 226
- Abscess, chronic typhoid, of ovary, (Soloff and Hermann), 290
- Abstracts, disease of respiratory and circulatory systems and intestinal tract complicating pregnancy, 305
- miscellaneous, 36, 75, 84, 123, 125, 128, 135, 144, 147, 158, 173, 198, 208, 220, 231, 248, 263, 280, 288, 300, 322, 338, 368, 379, 385, 391, 419, 424, 438, 523, 533, 543, 589, 595, 674, 695, 703, 709, 717, 723, 735, 762, 814, 840, 867
- organotherapy, 909
- radiography and radiotherapy, 603
- uterine carcinoma, 152, 303
- Adenocarcinoma and sarcoma of body of uterus, (Goldstine), 143
- of cervix, (Goldstine), 143
- of fundus of uterus, (Goldstine), 137
- Adnexitis, tuberculous, radiotherapy of, (Gilbert), 605 (Abst.)
- Agglutinins, passage of, into maternal milk, (Sodano), 84 (Abst.)
- Amenorrheas, hormone induction of menstruation in, of from three months' to nine years' duration, (Dunn), 186
- American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, 760 (Item)
- Board of Obstetrics and Gynecology, 455, 608 (Items)
- examination of, 457, 759 (Items)
- Committee on Maternal Welfare, (Adair), 868
- Gynecological Society, 154 (Item)
- transactions of, 736, 872
- Medical Association, 154 (Item)
- Amniotin in treatment of gonococcal vaginitis in children, experiences with, (Telinde and Brawner), 512, 887
- Analgesia and anesthesia in labor, (Lloyd-Williams), 751 (Book review)
- Obstetric, current techniques for, (Gould and Hirst), 257
- Anencephalic monster complicated by impacted ovarian cyst, (Rudolph), 865
- twins, (Litt and Strauss), 728
- Anesthesia and analgesia in labor, (Lloyd-Williams), 754 (Book review)
- obstetric, current techniques for, (Gould and Hirst), 257
- Intravenous, with cervical soluble, (Holman and Mathien), 118
- spinal, in ectopic pregnancy, value of, results of immediate operation and, (Koster and Sheinfeld), 93
- Announcement, 908
- Anterior lobe of pituitary, effect of administration of preparations of growth hormone of, upon gestation and weight of newborn (albino rats), (Watts), 171

- Antihormones, ovary-stimulating factors and, (Fluhmann), 584, 891
- Antisepsis, vaginal, during labor, mercurochrome to secure, (Mayes), 80
- Aplasia, vaginal, and creation of artificial vagina, (Israel), 273
- Appendicitis in gynecology, (Mitsui), 419 (Abst.)
- in pregnancy, (Marbury), 306 (Abst.)
- Arquivo de Patologia Orgao do Instituto Portugues Para O Estudo do Cancro, (Gentil and Athias), 442 (Book review)

## B

- Babies, healthy, are happy babies, (Kenyon), 447 (Book review)
- Basal metabolism study of 600 cases, (Davis), 570, 742
- Benign disease, vaginal hysterectomies performed for, a series of 627, with three deaths, (Heaney), 269
- lesions of cervix uteri, results of treatment of, (Tompkins), 369
- Bilateral peripheral paralysis of radial nerve in newborn infant, (Smith), 283
- Birth control, (Bromley), 756 (Book review)
- live, radiographic evidence of, (Hajkis), 604 (Abst.)
- trauma in cancer of uterine cervix, factor of, (Macfarlane), 133
- Bitterling test for pregnancy, value of, 155 (Correspondence)
- Bladder, elusive ulcer of, treatment of, by application of pure phenol, (Sears), 85
- Blastomycosis of female reproductive tract, (Hamblen, Baker, and Martin), 345
- Bleeding, corpus, in old women, (Schultz), 152 (Abst.)
- Blood, cell volume of, in nonpregnant and pregnant women, (Oberst and Woods), 232
- fibrinogen content of, of newborn babies, (Naeslund), 379 (Abst.)
- lipids in eclampsia, (Boyd), 323
- loss during cesarean section, (Dieckmann and Daily), 221
- oxygen content and capacity of, in nonpregnant and pregnant women, (Oberst and Woods), 232
- pressure, artificial reduction of, by trauma, effects of injection of 50 per cent glucose solution before and after, (Mazzola and Torrey), 339
- transfusion in treatment of obstetric hemorrhage, rôle of, (Dieckmann and Daily), 1
- Bloodless circumcision of newborn, (Yellen), 146
- Bone formation, heteroplastic, myofibroma of ovary with, (Stein), 289
- Book reviews, 441, 752
- Books received, 308, 458, 761
- Breuer tumor of ovary, (Smith), 734
- Broad ligament, lipoma of, (Kanter), 296
- Brooklyn Gynecological Society, transactions of, 151, 751
- Bullettino della società piemontese, (Percaro), 608 (Abst.)

\*July, pp. 1-158; August, pp. 159-308; September, pp. 309-458; October, pp. 459-608; November, pp. 609-762; December, pp. 763-925.



## C

- Cancer and estrogenic substances, relationship between, (Dodds), 301 (Editorial)
- and ulcer of stomach as complications of labor, (Gröné), 307 (Abst.)
- of cervix and hereditary syphilis, (Pauco), 303 (Abst.)
- and vagina in a case of complete procidentia, (Brady), 277
- detection of clinically latent, (Graves), 304 (Abst.)
- in cases of uterine prolapse, (Tourneux), 152 (Abst.)
- radium treatment of, during pregnancy, (Nielsen), 607 (Abst.)
- of female urethra, (Auer), 318
- of uterine cervix, factor of birth trauma in, (Macfarlane), 133
- histologic classification of, (Chambers), 154 (Abst.)
- of uterus in childhood, (Lockhart), 76
- uterine, statistics of, (Terada), 135 (Abst.)
- Carcinoma of cervix, pregnancy complicated by, (Neill), 414
- Schauta-Stoeckel vaginal radical operation for, permanent results of, (Schilling), 280 (Abst.)
- treatment of, by Wertheim's operation, (Bonney), 815
- of portio, coincidence of uterine prolapse and, (Haegler), 153 (Abst.)
- of tube, (Vignes), 288 (Abst.)
- of uterine cervix, histologic grading in, (Jorstad and Auer), 153 (Abst.)
- ovarian, inoperable, roentgen ray and radium treatment of, (Vogt), 607 (Abst.)
- primary, of fallopian tube, (Dannreuther), 724
- of hymen, (Nicholson and Calatroni), 220 (Abst.)
- squamous cell, of cervix, (Goldstine), 137
- stump, question of, (Hann), 304 (Abst.)
- uterine, 152 (Abst.)
- Cardiac disease, pregnancy complicating, (Daleman and Kornfeld), 386
- Castration, roentgen ray, indications, results and failures of, (Jacobi and Lindner), 606 (Abst.)
- Cauterization of cervix uteri, complications following, (Cannell and Douglass), 376
- Cell volume of blood in nonpregnant and pregnant women, (Oberst and Woods), 232
- Central Association of Obstetricians and Gynecologists, 760 (Item)
- Cervical erosions, vaginal insulin treatment of, theory and results of, (Klaften), 543 (Abst.)
- mucosa, leucoplakia of, etiology and malignant degeneration of, (Kolegajew), 303 (Abst.)
- Cervix, adenocarcinoma of, (Goldstine), 143
- cancer of, and hereditary syphilis, (Pauco), 303 (Abst.)
- and vagina in a case of complete procidentia, (Brady), 277
- during pregnancy, radium treatment of, (Nielsen), 607 (Abst.)
- in cases of uterine prolapse, (Tourneux), 152 (Abst.)
- carcinoma of, pregnancy complicated by, (Neill), 414
- treatment of, by Wertheim's operation, (Bonney), 815
- embryonal cysts of, and their etiology with report of two cases, (Kotz), 854
- prenatal and postnatal, management of, (Castillo and Montgomery), 37
- squamous cell carcinoma of, (Goldstine), 137

## Cervix—Cont'd

- uteri, benign lesions of, results of treatment of, (Tompkins), 369
- cauterization of, complications following, (Cannell and Douglass), 376
- fibromyoma of, (Counsellor and Collins), 108
- sarcoma of, nonpolypoid, (Goldstine), 145
- tuberculosis of, (Counsellor and Collins), 830
- uterine, cancer of, factor of birth trauma in, (Macfarlane), 133
- histologic classification of, (Chambers), 154 (Abst.)
- Cesarean section, (Daily), 204
- accident after spinal anesthesia for, an exceptional secondary, (Fournier), 523 (Abst.)
- analysis of 381 cases, in ten-year period at Michael Reese Hospital, (Stein and Leventhal), 192
- blood loss during, (Dieckmann and Daily), 221
- delivery by, a case of chondrodystrophic nanism with, (Balasquide), 430
- extraperitoneal (Latzko), review of 26 cases of, (Norton), 209
- factors influencing mortality, (Bowers), 103
- massive collapse of lung following, (Gustafson), 425
- porro, (Lash and Cummings), 199
- statistics in Chicago hospitals, 298
- Chemistry of hormones, (Harrow and Sherwin), 442 (Book review)
- Chicago Gynecological Society, transactions of, 151, 299, 751
- Children, diseases of, 447 (Book review)
- Chorionepithelioma and hydatidiform mole, (Mazza and de la Colina), 125 (Abst.)
- following full-term pregnancy, (Lull), 730
- Circumcision, bloodless, of newborn, (Yellen), 146
- Colpectomy in treatment of uterine and vaginal prolapse, place of, (Phaneuf), 544, 872
- Colposcope in gynecology, use of, (Preisacker), 144 (Abst.)
- new, (Maryan), 148
- Conception period of women, (Ogino), 445 (Book review)
- Conjugate, diagonal, new instrument for accurate reading of measurement of, (Douglas), 141
- Cord, multiple true knots in, (Litt and Strauss), 728
- Corpus bleeding in old women, (Schultz), 152 (Abst.)
- luteum, physiology of, (Allen and Reynolds), 309
- tumor, (Cutler), 131
- Correspondence, 155, 451, 452
- Curettage in young women, metrorrhagia and, (Quénu and Bédère), 595 (Abst.)
- Cyst, echinococci, of liver during pregnancy, (Superbi), 438 (Abst.)
- embryonal, of cervix and their etiology with report of two cases, (Kotz), 854
- ovarian, impacted, anencephalic monster complicated by, (Rudolph), 865
- twisted, ovarian, (Davidson), 128 (Abst.)

## D

- Delivery by cesarean section, case of chondrodystrophic nanism with, (Balasquide), 430
- forceps, primiparous perineum after, (Nugent), 249
- of living child, abdominal pregnancy with, (Posner), 293

F

Delivery—Cont'd

- spontaneous versus prophylactic methods of, analysis of end-results of labor in primiparas after, (Aldridge and Watson), 554, 595
- Diabetes and pregnancy, some problems in, (Kramer), 68
- Diagonal conjugate, new instrument for accurate reading of measurement of, (Douglas), 141
- Diameter of pelvis, true conjugate, simple roentgenographic method for accurately determining, (Witzner), 126
- Dilaudid in gynecologic surgery, use of, (Brown and Kleine), 89
- Disease, nomenclature of, standard classified, 450 (Book review)
- Dorn and Sugarman, sex predilection test of, (Pommerenke and Rogers), 380
- Dysmenorrhea, treatment of, by presacral sympathectomy, (Keene), 534, 740

E

- Echinococcal cyst of liver during pregnancy, (Superbi), 438 (Abst.)
- Eclampsia and preeclampsia, protein stabilization in, (Harden, McElroy, and Huggins), 524
- blood lipids in, (Boyd), 323
- veratrum viride in treatment of, (Bryant), 46
- Ectopic pregnancy; (Koster and Sheinfeld), 93
- Electrouterography, (Falk and Nahon), 403
- Embryology, experimental, elements of, (Huxley and de Beer), 445 (Book review)
- Embryonal cysts of cervix and their etiology with report of two cases, (Kotz), 854
- Endocrine factors of lactation, (Kabak and Kizelshtein), 913 (Abst.)
- headaches, (Sure), 911 (Abst.)
- Endocrinology, 441 (Book review)
- practical, (Goldzieher), 442 (Book review)
- recent advances in, (Camerson), 441 (Book review)
- Endocrinopathies, homotransplantation as a method of treatment of, (Arapoff), 912 (Abst.)
- Endometrial hyperplasia, (Burch, Phelps, and Wolfe), 123 (Abst.)
- Endometritis, tuberculous, (Diethelm and Ramsey), 420
- Endometrium, diffuse sarcoma of, (Moench and Meeker), 435
- Epithelioma, uterine, gonadotropic hormone in, experimental researches on, (Cornil and Escarras), 914 (Abst.)
- Ergot derivative, ergotocin, study of new and potent, (Adair, Davis, Kharsch, and Legault), 466, 740
- oxytocic principle of, clinical test of newly recognized, and new method of administration, (Tuck), 718
- Ergotocin, ergot derivative, study of new and potent, (Adair, Davis, Kharsch, and Legault), 466, 740
- Estrogenic substances and cancer, relationship between, (Dodds), 301 (Editorial)
- Estrus-producing hormones, (Dodds), 909 (Abst.)
- Evipal soluble, intravenous anesthesia with, (Holman and Mathieu), 118
- Excoriation of perineum from silver wire sutures, prevention of, (Grad), 863
- Extraperitoneal (Latzko) cesarean section, review of 26 cases of, (Norton), 209
- Extrauterine pregnancy, (Fitzgerald and Brewer), 264

- Facies Dolorosa, (Killian), 757 (Book review)
- Fallopian tube, lipoma of, (Bagetti), 695 (Abst.)
- primary carcinoma of, (Dannreuther), 724
- Female allments, treatment of common, (McCann), 754 (Book review)
- Fetal mortality in patients with organic heart disease, study of, (Teel), 53
- Fetus papyraceous in twin pregnancy, (Crotty), 296
- Fever, puerperal, source of infection in, further investigation into, (Smith), 173 (Abst.)
- Fibrinogen content of blood of newborn babies, (Naeslund), 379 (Abst.)
- Fibromyoma of cervix uteri, (Connseiler and Collins), 108
- Fistulas, vesicovaginal, treatment of, (Miller), 675
- Follicular hormone, use of, in premature infants, (Brochier), 911 (Abst.)
- Forceps delivery, primiparous perineum after, (Nugent), 249
- Fothergill operation, technic, 157 (Correspondence)
- Friedman rabbit ovulation test in differential obstetric diagnosis, (King), 735 (Abst.)
- Frommel's disease, uteroovarian atrophy with persistent inaction, historical review of syndrome embracing, (Sharp), 411
- Fundus of uterus, adenocarcinoma of, (Goldstine), 137

G

- Galactin and thceiin, experiments with, on growth and function of mammary glands of monkey, (Allen Gardner, and Diddle), 912 (Abst.)
- Gangrene, intrauterine gas, with recovery, (Carroll), 858
- Genitalia, female, effects of an accident on, (Mayer), 449 (Book review)
- Genitourinary diseases, synopsis of, (Dobson), 757 (Book review)
- system, x-ray treatment of diseases of, (Orton), 840 (Abst.)
- Gestation, tubal, (Tyrono, Romano, and Collins), 112
- Glucose, hypertonic, solution (50 per cent), intravenous injections of, experimental study of effects of, on circulation of cat, (Mazzoin and Torrey), 339
- Glutathione of blood in nonpregnant and pregnant women, (Oberst and Woods), 723
- studies in, (Oberst and Woods), 232
- Gonococcal vaginitis in children, experiences with amniotin in treatment of, (Telinde and Brawner), 512, 887
- Gonorrhea in females, pathologic diagnosis of, (Maseall), 248 (Abst.)
- routine treatment of, (Notes), 121
- Gonorrheal vaginitis, pyridium in treatment of, in children, (Brown et al.), 198 (Abst.)
- Great Britain, contributions of, to gynecology and obstetrics, (Anspach), 459
- Gynecologic hormone therapy, progress in, (Buschbeck), 909 (Abst.)
- surgery, use of dilaudid in, (Brown and Kleine), 89
- Gynecology, (Anspach), 752 (Book review)
- abruptio placentae, treatment of, (McGlinn and Harer), 226
- abscess, chronic typhoid, of ovary, (Soloff and Herrmann), 290

## Gynecology—Cont'd

- adenocarcinoma and sarcoma of body of uterus, (Goldstine), 143  
 of cervix, (Goldstine), 143  
 of fundus of uterus, (Goldstine), 137  
 amenorrheas, hormonal induction of menstruation in, of from three months' to nine years' duration, (Dunn), 186  
 and obstetrics, 752 (Book review)  
 contributions of Great Britain to, (Anspach), 459  
 appendicitis in, study of, (Mitsui), 419 (Abst.)  
 benign lesions of cervix uteri, results of treatment of, (Tompkins), 369  
 blastomycosis of female reproductive tract, (Hamblen, Baker, and Martin), 345  
 cancer of cervix and hereditary syphilis, (Paucoot), 303 (Abst.)  
 and vagina in case of complete procidentia, (Brady), 277  
 of female urethra, (Auer), 318  
 of uterine cervix, factor of birth trauma in, (Macfarlane), 133  
 of uterus in childhood, (Loekhart), 76  
 uterine, statistics of, (Tcrada), 135 (Abst.)  
 carcinoma of cervix, pregnancy complicated by, (Neill), 414  
 treatment of, by Wertheim's operation, (Bonney), 815  
 of tube, (Vignes), 288 (Abst.)  
 of uterine cervix, histologic grading in, (Jorstad and Auer), 153 (Abst.)  
 primary, of fallopian tube, (Dannreuther), 724  
 of hymen, (Nicholson and Calatroni), 220 (Abst.)  
 squamous cell, of cervix, (Goldstine), 137  
 stump, question of, (Hann), 304 (Abst.)  
 uterine, 152 (Abst.)  
 cauterization of cervix uteri, complications following, (Cannell and Douglass), 376  
 chorionepithelioma following full-term pregnancy, (Lull), 730  
 colposcope in, use of, (Preisseecker), 144 (Abst.)  
 new, (Maryan), 148  
 cysts, embryonal, of cervix and their etiology with report of two cases, (Kotz), 854  
 ovarian, impacted, anencephalic monster complicated by, (Rudolph), 865  
 dysmenorrhea, treatment of, by presacral sympathectomy, (Keene), 534, 740  
 endometritis, tuberculous, (Diethelm and Ramsey), 420  
 fibromyoma of cervix uteri, (Counseller and Collins), 108  
 fistulas, vesiovaginal, treatment of, (Miller), 675  
 gonorrhea in females, pathologic diagnosis of, (Maseall), 248 (Abst.)  
 routine treatment of, (Notes), 121  
 gonorrheal vaginitis, pyridium in treatment of, in children, (Brown et al.), 198 (Abst.)  
 hematometra, (McGinn and Harer), 704  
 hemorrhage after menopause and exploratory curettage, (Burger), 304 (Abst.)  
 uterine, (Witherspoon), 762 (Abst.)  
 hysterectomies, vaginal, performed for benign disease with three deaths, series of 627, (Heaney), 269  
 hysterectomy, abdominal, in benign uterine disease, total versus subtotal, (Richardson), 237  
 hystero-graphy, recent advances in, (Menees and Miller), 590, 887

## Gynecology—Cont'd

- inversion of uterus in two successive pregnancies, (Fox), 295  
 lipoma of broad ligament, (Kanter), 296  
 melanoma of urethra, (Rosenthal), 115  
 menstrual disorders, functional, therapeutic value of low-dosage irradiation of pituitary gland and ovaries in, (Mazer and Spitz, Jr.), 214  
 metrorrhagia among young women, (Béclère), 604 (Abst.)  
 in menopause, (Guyot, Courriades, and Roher), 391 (Abst.)  
 in young women and curettage, (Quénu and Béclère), 595 (Abst.)  
 x-ray treatment in certain forms of, (Husted), 606 (Abst.)  
 myofibroma of ovary with heteroplastic bone formation, (Stein), 289  
 myomectomy, extended scope of, (Bonney), 746  
 operative, tribromethynol premedication in, (Reveraff), 332  
 ovarian cyst, twisted, (Davidson), 128 (Abst.)  
 dysfunctions, surgical treatment of, (Robinson), 18  
 tumors, histogenesis of certain, and their biologic effects, (Geist), 650  
 procidentia, complete, cancer of cervix and vagina in case of, (Brady), 277  
 prolapse, uterine and vaginal, colpectomy in treatment of, place of, (Phaneuf), 544, 872  
 prophylaxis in, (Goff), 878  
 psychosis, puerperal, and mastitis, (Ito), 368 (Abst.)  
 reimplantation, tubal—in retrospect, (Tarnowsky), 696  
 retrodisplacement of uterus, when is surgery indicated in, (Gardner), 596, 749  
 retroversion of uterus, (Luker), 300 (Abst.)  
 roentgen ray in, value of, (Jarcho), 604 (Abst.)  
 salpingitis isthmica nodosa, human ovum in, (Lash), 287  
 sarcoma and adenocarcinoma of body of uterus, (Goldstine), 143  
 diffuse, of endometrium, (Moeneh and Meeker), 435  
 nonpolypoid, of cervix uteri, (Goldstine), 145  
 textbook of, (Curtis), 752 (Book review)  
 trichomonas vaginitis, clinical and bacteriologic observations in, (Allen, Jensen, and Wood), 565, 736  
 tubal reimplantation—in retrospect, (Tarnowsky), 696  
 tuberculosis of cervix uteri, (Counseller and Collins), 830  
 tumors, Brenner, of ovary, (Smith), 734  
 corpus luteum, (Cutler), 131  
 of female pelvic organs, (Meigs), 449 (Book review)  
 ovarian, histogenesis of certain, and their biologic effects, (Geist), 650  
 uterine disease, benign, total versus subtotal abdominal hysterectomy in, (Richardson), 237  
 vaginitis, gonococcal, in children, experiences with amniotin in treatment of, (TeLinde and Brawner), 512, 887

## H

- Headache, endocrine, (Sure), 911 (Abst.)  
 pituitary, (Skipp), 911 (Abst.)  
 Heart disease complicating pregnancy, review of 190 cases of, (Hanley and Anderson), 243  
 in pregnancy, (Lamb), 305 (Abst.)

## Heart Disease—Cont'd

- organie, fetal mortality in patients with, study of, (Teel), 53  
rheumatic, does pregnancy hasten fatal termination in, (Glehlrist and Murray-Lyon), 305 (Abst.)  
Hematometra, (McGlinn and Harer), 701  
Hemorrhage after menopause and exploratory curettement, (Burger), 304 (Abst.)  
in late pregnancy, (Smith), 62  
obstetric, blood transfusion in treatment of, rôle of, (Dieckmann and Daily), 1  
postmenopausal, an analysis of 937 cases of, (Fahmy), 152 (Abst.)  
traumatic, from vagina, (Ghosh), 703 (Abst.)  
uterine, (Witherspoon), 762 (Abst.)  
Hernia, congenital umbilical, operative treatment of, (Ludwig), 208 (Abst.)  
Hirst, Barton Cooke, in memoriam, 609  
Homotransplantation as method of treatment of endocrinopathies, (Arapoff), 912 (Abst.)  
Hormone, chemistry of, (Harrow and Sherwin), 442 (Book review)  
estrus-producing, (Dodds), 909 (Abst.)  
follicular, use of, in premature infants, (Broehier), 911 (Abst.)  
gonadotropic, in uterine epithelioma, experimental researches on, (Cornil and Escarras), 914 (Abst.)  
growth, of anterior lobe of pituitary, effect of administration of preparations of, upon gestation and weight of newborn (albino rats), (Watts), 174  
therapy, progress in gynecology, (Buschbeck), 909, 910 (Absts.)  
und innere sekretion, (Laqueur), 441 (Book review)  
Hormone Induction of menstruation in amenorrheas of from three months' to nine years' duration, (Dunn), 186  
Hydatidiform mole and chorionepithelioma, (Mazza and de la Colina), 125 (Abst.)  
Hymen, primary carcinoma of, (Nicholson and Calatroni), 220 (Abst.)  
Hyperplasia, endometrial, (Burch, Phelps, and Wolfe), 123 (Abst.)  
Hypoglycemic substances, action of, upon certain fermentative processes of neoplastic tissue, (Gentil and Athias), 442 (Book review)  
Hypophysectomized patients, clinical observation on, (Borovskaja), 911 (Abst.)  
Hypophysectomy, partial, Zondek-Aschheim test after, (Stern), 912 (Abst.)  
Hypothyroidism as problem in women, (Davis), 570, 742  
Hysterecemies, vaginal, performed for benign disease with three deaths, series of 627, (Heaney), 269  
Hysterectomy, abdominal, in benign uterine disease, total versus subtotal, (Riehardson), 237  
Hysterography, recent advances in, (Menees and Miller), 590, 887  
Hysterosalpingography, accidental vascular injection in course of, (Bélère), 604 (Abst.)

## I

- In memoriam, Barton Cooke Hirst, (Nicholson), 609  
Infant, newborn, bilateral peripheral paralysis of radial nerve in, (Smith), 283  
Infertility, periodic, in women, question of, (Schumacher), 424 (Abst.)  
Injection, accidental vascular, in course of hysterosalpingography, (Bélère), 604 (Abst.)

## Injection—Cont'd

- of varicose veins during pregnancy, (Cheatham and Peek), 392  
Instrument for accurate reading of measurement of diagonal conjugate, new, (Douglas), 141  
Insulin treatment, vaginal, of cervical erosions, theory and results of, (Klaften), 543 (Abst.)  
Inversion of uterus in two successive pregnancies, (Fox), 295  
Interstitial pregnancy, ruptured, (Weinstein), 849  
Intestinal canal during normal pregnancy, influence of position and function of, (Guthmann and Stahler), 158 (Abst.)  
Intrauterine gas gangrene with recovery, (Carrell), 858  
Intravenous anesthesia with evlpal soluble, (Holman and Mathieu), 118  
injection of hypertonic glucose solution (50 per cent) on circulation of cat, experimental study of effects of, (Mazzola and Torrey), 339  
of thorium preparations, histologic changes in rabbits and in dogs following, (Shute and Davis), 605 (Abst.)  
Introduzione allo Studio Dell' Eugènea, (Cristalli), 446 (Book review)  
Item, American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, 760  
Board of Obstetrics and Gynecology, 455, 608, 759  
Gynecological Society, 154  
Medical Association, 154  
Central Association of Obstetricians and Gynecologists, 760  
Pacific Coast Society of Obstetrics and Gynecology, 151

## K

- Krukenberg tumors, pathogenesis of, (Pulir), 589 (Abst.)

## L

- Labor, anesthesia and analgesia in, (Lloyd-Williams), 754 (Book review)  
complicated by cancer and ulcer of stomach, (Gröné), 307 (Abst.)  
in primiparas, analysis of end-results of, after spontaneous versus prophylactic methods of delivery, (Aldridge and Watson), 554, 895  
in young and old primiparas, a parallel study of, (Nathanson), 159  
girls, an analysis of, (Posner and Pulver), 357  
mechanism of, further studies on, (Caldwell, Moloy, and D'Esopo), 763, 872  
painless, control of restlessness in, (Bartholomew), 866  
presentation, transverse, spontaneous evolution of, (Fraser), 732  
rupture of membranes, determination of, (King), 860  
vaginal antiseptics during, mereurochrome to secure, (Mayes), 80  
Lactation, endocrine factors of, (Kabak and Kizelshtein), 913 (Abst.)  
persistent, historical review of syndrome embracing uteroovarian atrophy with, (Sharp), 411  
physiology of, studies of, (Nelson), 147 (Abst.)  
Latzko (extraperitoneal) cesarean section, review of 26 cases of, (Norton), 209  
Leucoplakia of cervical mucosa, etiology and malignant degeneration of, (Kolegajew), 303 (Abst.)  
Levulose, metabolism of, (Rowe, McManus, and Riley), 841  
Ligament, broad, lipoma of, (Kanter), 296

- Lipids, blood, in eclampsia, (Boyd), 323  
 Lipoma of broad ligament, (Kanter), 296  
 of fallopian tube, (Bagetti), 695 (Abst.)  
 Lithopedion, six months', abdominal pregnancy with removal after eighteen years of, (Voegelín), 129  
 Lung, massive collapse of, following cesarean section, (Gustafson), 425  
 Lungentuberkulose und Schwangerschaft, (Braeuning), 444 (Book review)

## M

- Malignant diseases of uterus and ovaries, roentgen therapy in, experience with multiple doses, (Hcaly), 613, 904  
 Mammary glands, experiments with theelin and galactin on growth and function of, of monkey, (Allen, Gardner, and Diddle), 912 (Abst.)  
 Manobras e Operacoes Obstetricas, (Camargo), 443 (Book review)  
 Mastitis and puerperal psychosis, (Ito), 368 (Abst.)  
 Maternal milk and menstruation, (Stelnert and Papp), 75 (Abst.)  
 passage of agglutinins into, (Sodano), 84 (Abst.)  
 mortality in Philadelphia, 445 (Book review)  
 in Rochdale, (Oxley, Phillips and Young), 723 (Abst.)  
 welfare, American committee on, (Adair), 868  
 department of, 298, 439, 868  
 Medicine, economic problems of, (Christie), 755 (Book review)  
 in America, Jewish contributions to, (Kagan), 450 (Book review)  
 Melanocyte reaction of preparations of pituitary body and urine of cancer patients, (Umecawa), 914 (Abst.)  
 Melanoma of urethra, (Rosenthal), 115  
 Membranes, rupture of, determination of, (Kling), 860  
 Menopause, hemorrhages after, and exploratory curettement, (Burger), 304 (Abst.)  
 metrorrhagia in, (Guyot, Courriades, and Roher), 391 (Abst.)  
 Menstrual disorder, functional, therapeutic value of low-dosage irradiation of pituitary gland and ovaries in, (Mazer and Spitz), 214  
 response to luteinizing extract of pregnant urine, (Murphy, Shoemaker, and Rea), 910 (Abst.)  
 Menstruation, artificial production of, with ovarian hormones in cases of primary and secondary amenorrhea, (Locser), 910 (Abst.)  
 hormonal induction of, in amenorrheas of from three months' to nine years' duration, (Dunn), 186  
 maternal milk and, (Stelnert and Papp), 75 (Abst.)  
 Mercurochrome to secure vaginal antisepsis during labor, (Mayes), 80  
 Metabolism, basal, study of 600 cases, (Davis), 570, 742  
 of levulose, (Rowe, McManus, and Riley), 841  
 Metrorrhagia among young women, (Béclère), 604 (Abst.)  
 in menopause, (Guyot, Courriades, and Roher), 391 (Abst.)  
 in young women and curettage, (Quénu and Béclère), 595 (Abst.)  
 x-ray treatment in certain forms of, (Husted), 606 (Abst.)  
 Milk, maternal, passage of agglutinins into, (Sodano), 84 (Abst.)  
 Monoamniotic twins, one normal, other anencephalic, (Litt and Strauss), 728  
 Monster, anencephalic, complicated by impacted ovarian cyst, (Rudolph), 865

## Monster—Cont'd

- in successive pregnancies, an instance of like, (DerBruecke), 429  
 Mortality, factors influencing, cesarean section, (Bowers), 103  
 fetal, in patients with organic heart disease, study of, (Tecl), 53  
 maternal, in Philadelphia, 445 (Book review)  
 in Rochdale, (Oxley, Phillips, and Young), 723 (Abst.)  
 Mother, prospective, (Simmons), 446 (Book review)  
 Motility in transplanted, denervated uterus, (Kaminester, and Reynolds), 395  
 Myofibroma of ovary with heteroplastic bone formation, (Stein), 289  
 Myomeotomy, extended scope of, (Bonney), 746

## N

- Nanism, chondrodystrophie, ease of, with delivery by cesarean section, (Balasquide), 430  
 Nerve, radial, bilateral peripheral paralysis of, in newborn infant, (Smith), 283  
 New York Obstetrical Society, transactions of, 751  
 Newborn, bloodless circumcision of, (Yellen), 146  
 effect of administration of preparations of growth hormone of anterior lobe of pituitary upon gestation and weight of, (albino rats), (Watts), 174  
 Nomenclature of disease, standard classified, 450 (Book review)  
 Nonpolypoid sarcoma of cervix uteri, (Goldstine), 145  
 Nursing, technique, textbook of, (Vannier and Thompson), 450 (Book review)

## O

- Obstetrical Society of Philadelphia, transactions of, 151, 751  
 Obstetrics, 443 (Book review)  
 aids to, (Williams), 444 (Book review)  
 analgesia and anesthesia, current techniques for, (Gould and Hirst), 257  
 and gynecology, 752 (Book review)  
 contributions of Great Britain to, (Anspach), 459  
 cesarean section, (Dally), 204  
 analysis of 381 cases, at Michael Reese Hospital, (Stein and Leventhal), 192  
 blood loss during, (Dieckmann and Dally), 221  
 extraperitoneal (Latzko), review of 26 cases of, (Norton), 209  
 factors influencing mortality, (Bowers), 103  
 massive collapse of lung following, (Gustafson), 425  
 delivery by cesarean section, case of chondrodystrophic nanism with, (Balasquide), 430  
 eclampsia, blood lipids in, (Boyd), 323  
 veratrum viride in treatment of, (Bryant), 46  
 forceps delivery, primiparous perineum after, (Nugent), 249  
 gestation, tubal, (Tyroné, Romano, and Collins), 112  
 hemorrhage, blood transfusion in treatment of, rôle of, (Dieckmann and Dally), 1  
 labor complicated by cancer and ulcer of stomach, (Grüné), 307 (Abst.)  
 in primiparas, analysis of end-results of, after spontaneous versus prophylactic methods of delivery, (Aldridge and Watson), 554, 895  
 in young and old primiparas, parallel study of, (Nathanson), 159

## Obstetrics, Labor—Cont'd

- in young girls, analysis of, (Posner and Pulver), 357
- mechanism of, further studies on, (Caldwell, Moloy, and D'Esopo), 763, 872
- painless, control of restlessness in, (Bartholomew), 866
- occiput posterior, (Crotty), 97
- occipitoposterior position, treatment of persistent, by 180 degree manual rotation of occiput, (Rosenfeld), 364
- porro cesarean section, (Lash and Cummings), 199
- pregnancies, successive, instance of like monsters in, (DerBrucke), 429
- pregnancy, abdominal, with delivery of living child, (Posner), 293
  - with removal, after eighteen years, of six months' lithopedion, (Vocgelin), 129
- complicated by carcinoma of cervix, (Neill), 414
- complicating cardiac disease, (Daichman and Kornfeld), 386
- ectopic, (Koster and Scheinfeld), 93
- extrauterine, (Fitzgerald and Brewer), 264
- full-term, chorionepithelioma following, (Lull), 730
- heart disease in, (Lamb), 305 (Abst.)
  - complicating, review of 190 cases of, (Hanley and Anderson), 243
- in patient with complete double uterus, (Green and Miller), 281
- late, hemorrhage in, (Smith), 62
- ovarian, (Holloway), 286
- ruptured interstitial, (Weinstein), 849
- toxemia of, (Goodall), 577, 876
- twin, fetus papyraceous in, (Crotty), 296
  - full-term unilateral tubal, (Ferguson and Otis), 139
- urinary tract during, physiologic changes occurring in, (Hundley, Walton, Hibblits, Siegel, and Brack), 625, 885
- varicose veins during, injection of, (Cheatham and Peck), 392
- roentgenology in, (Wahl), 603 (Abst.)
- rupture of membranes, determination of, (King), 860
- toxemias of late pregnancy, (Thomas, Allen, Bauer, and Freeland), 665
- of pregnancy, (Goodall), 577, 876
- transverse presentation, spontaneous evolution of, (Fraser), 732
- x-ray picture indicated in, when is an, (Heyrowsky), 603 (Abst.)
- Occipitoposterior position, treatment of persistent, by 180 degree manual rotation of occiput, (Rosenfeld), 364
- Occiput posterior, (Crotty), 97
- Operations, surgical, names of, (Black), 755 (Book review)
- Operative gynecology, tribromethanol premedication in, (Reycraft), 332
- Opuscula Selecta Neerlandicorum de Arte Medica, 444 (Book review)
- Organotherapy, 909 (Abst.)
- Ovarian carcinoma, inoperable, roentgen ray and radium treatment of, (Vogt), 607 (Abst.)
  - conditions as causes of pelvic pain, (Davidson), 36 (Abst.)
- cyst, impacted, anencephalic monster complicated by, (Rudolph), 865
- twisted, (Davidson), 128 (Abst.)
- dysfunction, sterility due to, (Jeffcoate), 913 (Abst.)
  - surgical treatment of, (Robinson), 18
- hormones, artificial production of menstruation with, in cases of primary and secondary amenorrhea, (Loeser), 910 (Abst.)

## Ovarian—Cont'd

- pregnancy, (Holloway), 286
  - preparations, influence of, upon general development of fetuses at term, (Macchiarulo), 911 (Abst.)
  - tumors, histogenesis of certain, and their biologic effects, (Geist), 650
  - Ovaries and uterus, malignant diseases of, experience with multiple dose roentgen therapy in, (Healy), 613, 904
    - in functional menstrual disorders, therapeutic value of low-dosage irradiation of pituitary gland and, (Mazer and Spitz), 214
  - Ovary, Brenner tumor of, (Smith), 734
  - chronic typhoid abscess of, (Soloff and Hermann), 290
  - myofibroma of, with heteroplastic bone formation, (Stein), 289
  - stimulating factors and antihormones, (Fluhmann), 584, 891
  - tumors of, (Gery and Adrian), 674 (Abst.)
  - Ovulation, consideration of phenomenon of, and its relation to sex cycle, (Stein), 710
  - test, Friedman rabbit, in differential obstetric diagnosis, (King), 735 (Abst.)
  - Ovum, human, in salpingitis isthmica nodosa, (Lash), 287
  - Oxygen content and capacity of blood in nonpregnant and pregnant women, (Oberst and Woods), 232
  - Oxytocic principle of ergot, clinical test of newly recognized, and new method of administration, (Tuck), 718
- P
- Pacific Coast Society of Obstetrics and Gynecology, 154 (Item)
  - Paralysis, bilateral peripheral, of radial nerve in newborn infant, (Smith), 283
  - Parenthood, (Fielding), 757 (Book review)
  - Pediatrics, synopsis of, (Zahorsky), 448 (Book review)
  - Pelvic organs, female, tumors of, (Meigs), 449 (Book review)
  - pain, ovarian conditions as causes of, (Davidson), 36 (Abst.)
  - Pelvis, kyphotic, patients with, torsion of pregnant uterus in, (Rabbiner), 136
    - true conjugate diameter of, roentgenographic method for accurately determining, (Weitzner), 126
  - Perineum, excoriation of, from silver wire sutures, prevention of, (Grad), 863
  - primiparous, after forceps delivery, (Nugent), 249
  - Phenol, application of pure, treatment of elusive ulcer of bladder by, (Sears), 85
  - Philadelphia Obstetrical Society, transactions of, 299
  - Physiologische Chemie der Geburt, (Siedentopf), 754 (Book review)
  - Physiology, reproductive, some newer aspects of, (Novak), 495, 892
  - Pituitary, anterior lobe of, effect of administration of preparations of growth hormone of, upon gestation and weight of newborn (albino rats), (Watts), 174
    - body, melanocyte reaction of preparations of, and urine of cancer patients, (Umezawa), 914 (Abst.)
    - gland, low-dosage irradiation of, and ovaries in functional menstrual disorders, therapeutic value of, (Mazer and Spitz), 214
    - headache, (Skepp), 911 (Abst.)

- Placenta, premature partial separation of normally situated, nonsurgical parturition in three cases of, (Bazan and Roth), 231 (Abst.)
- Population, dynamics of, (Lorimer and Asborn), 756 (Book review)
- Porro cesarean section, (Lash and Cummings), 199
- Position, occipitoposterior, treatment of persistent, by 180 degree manual rotation of occiput, (Rosenfeld), 364
- Postnatal and prenatal cervix, management of, (Castallo and Montgomery), 37
- Pratique Obstétricale, (Devraigne), 443 (Book review)
- Preeclampsia and eclampsia, protein stabilization in, (Harden, McEllroy, and Huggins), 524
- Pregnancies, inversion of uterus in two successive, (Fox), 295
- Pregnancy, abdominal, with delivery of living child, (Posner), 293  
with removal, after eighteen years, of six months' lithopedion, (Voegelin), 129  
after x-ray treatment of mother, (Tesauro), 606 (Abst.)  
and diabetes, some problems in, (Kramer), 69  
appendicitis in, (Marbury), 306 (Abst.)  
Bitterling test for, value of, 155 (Correspondence)  
cancer of cervix during, radium treatment of, (Nielsen), 607 (Abst.)  
complicated by carcinoma of cervix, (Neill), 414  
complicating cardiac disease, (Daehman and Kornfeld), 386  
diseases of respiratory and circulatory systems and intestinal tract complicating, 305 (Abst.)  
echinococcal cyst of liver during, (Superbi), 438 (Abst.)  
eclampsia and preeclampsia, protein stabilization in, (Harden, McEllroy, and Huggins), 524  
ectopic, (Koster and Sheinfeld), 93  
extrauterine, (Fitzgerald and Brewer), 264  
full-term, chorionepithelioma following, (Lull), 730  
heart disease in, (Lamb), 305 (Abst.)  
complicating, review of 190 cases of, (Hanley and Anderson), 243  
in patient with complete double uterus, (Green and Miller), 281  
interstitial, ruptured, (Weinstein), 849  
intestinal canal during normal, influence of position and function of, (Guttmann and Stahler), 158 (Abst.)  
labor, and puerperium, unexpected, sudden death of patient during, (Kehrer), 444 (Book review)  
late, hemorrhage in, (Smith), 62  
monsters in successive, an instance of like, (DerBrucke), 429  
ovarian, (Holloway), 286  
preeclampsia and eclampsia, protein stabilization in, (Harden, McEllroy, and Huggins), 524  
pyelitis of, postpartum, (Rose), 322 (Abst.)  
rupture of membranes, determination of, (King), 860  
toxemias of, (Oberst and Woods), 232: (Goodall), 577, 876  
of late, (Thomas, Allen, Bauer, and Freeland), 665  
tubal gestation, (Tyrone, Romano, and Collins), 112  
twin, full-term unilateral, (Ferguson and Otis), 139  
twin, fetus papyraceous in, (Crotty), 296
- Pregnancy—Cont'd  
urinary tract during, physiologic changes occurring in, (Hundley, Walton, Hibbitts, Siegel, and Brack), 625, 885  
urine, results of preoperative administration of an extract of, (Hamblen), 913 (Abst.)  
varicose veins during, injection of, (Cheatham and Peck), 392
- Pregnant uterus, torsion of, in patients with kyphotic pelvis, (Rabbiner), 136
- Premenstrual elevation of temperature, (v. Fekete), 385 (Abst.)
- Prenatal and postnatal cervix, management of, (Castallo and Montgomery), 37  
care, evaluation of, (Miller), 439  
report on evaluation of, (Watkins and Walker), 445 (Book review)
- Presacral sympathectomy, treatment of dysmenorrhea by, (Keene), 534, 740
- Presentation, transverse, spontaneous evolution of, (Fraser), 732
- Primiparas, labor in, analysis of end-results of, after spontaneous versus prophylactic methods of delivery, (Aldridge and Watson), 554, 895  
young and old labor in, parallel study of, (Nathanson), 159
- Primiparous perineum after forceps delivery, (Nugent), 249
- Procidencia, complete, cancer of cervix and vagina in case of, (Brady), 277
- Progestin, crystalline, and crude progestin, comparative actions of, on uterine motility in unanesthetized rabbits, (Allen and Reynolds), 309
- Prolapse, uterine and vaginal, colpectomy in treatment of, place of, (Phaneuf), 544, 872  
cancer of cervix in cases of, (Tourneux), 152 (Abst.)
- Propédeutique Obstétricale, (Devraigne), 443 (Book review)
- Prophylaxis in gynecology, (Goff), 878
- Prospective mother, (Slemons), 446 (Book review)
- Protein stabilization in preeclampsia and eclampsia, (Harden, McEllroy, and Huggins), 524
- Pruritus vulvae, etiologic and therapeutic consideration, (David-Chaussé), 533 (Abst.)  
treatment of, by infiltration with radon in pruritic area, (Gasquet), 717 (Abst.)
- Psychosis, puerperal, and mastitis, (Ito), 368 (Abst.)
- Puerperal fever, infection in, further investigation into the source of, (Smith), 173 (Abst.)  
psychosis and mastitis, (Ito), 368 (Abst.)
- Pulmonary tuberculosis, (Braeuning), 444 (Book review)
- Pyelitis, postpartum, of pregnancy, (Rose), 322 (Abst.)
- Pyridium in treatment of gonorrheal vaginitis in children, (Brown et al.), 198 (Abst.)
- R
- Radiographic evidence of live birth, (Hajkis), 604 (Abst.)
- Radiotherapy of tuberculous adnexitis, (Gilbert), 605 (Abst.)
- Radium and roentgen ray treatment of inoperable ovarian carcinoma, (Vogt), 607 (Abst.)  
treatment in cancers of uterine cervix, (Chambers), 154 (Abst.)  
of cancer of cervix during pregnancy, (Nielsen), 607 (Abst.)



Reimplantation, tubal—in retrospect, (Tarnowsky), 696  
 Reproductive cycle on toleranc, influence of, (Rowe, McManus, and Riley), 841  
     physiology, some newer aspects of, (Novak), 495, 892  
     tract, female, blastomycosis of, (Hamb-  
     len, Baker, and Martin), 345  
 Retrodisplacement of uterus, when is sur-  
 gery indicated in, (Gardner), 596, 749  
 Retroversion of uterus, (Luker), 300 (Abst.)  
 Review of new books, 441, 752  
 Rheumatic heart disease, does pregnancy hasten fatal termination in, (Gilchrist and Murray-Lyon), 305 (Abst.)  
     syndrome, autonomic diseases or, (Rivers), 758 (Book review)  
 Roentgen ray and radium treatment of inoperable ovarian carcinoma, (Vogt), 607 (Abst.)  
     castration, indications, results and failures of, (Jacobi and Lindner), 606 (Abst.)  
     in gynecology, value of, (Jarcho), 604 (Abst.)  
     therapy in malignant diseases of uterus and ovaries, experience with multiple dose, (Hcally), 613, 904  
 Roentgenology in obstetrics, (Wahl), 603 (Abst.)  
 Roentgenothérapie des fibronyomes de l'uterus, et de metropathies hemorragiques, (Gilbert), 753 (Book review)  
 Rupture of membranes, determination of, (King), 860

S

Salpingitis isthmica nodosa, human ovum in, (Lash), 287  
 Sarcoma and adenocarcinoma of body of uterus, (Goldstine), 143  
     diffuse, of endometrium, (Moeneli and Meeker), 435  
     nonpolypoid, of cervix uteri, (Goldstine), 145  
 Sex cycle, ovulation and its relation to, consideration of phenomenon of, (Stein), 710  
     prediction test of Dorn and Sugarman, (Pommerecke and Rogers), 380  
     ratio, normal, of albino rats, observa-  
     tions on, and their artificial varia-  
     tion, (Varzhahedian), 124  
 Society transactions, American Gynecological Society, 736, 872  
     Brooklyn Gynecological Society, 151, 751  
     Chicago Gynecological Society, 151, 299, 300, 751  
     New York Obstetrical Society, 751  
     Obstetrical Society of Philadelphia, 151, 299, 751  
     Washington Gynecological Society, 908  
 Speculum, vaginal, modified, (Fullerton), 297  
 Spinal anesthesia, accident after, for cesarean section, an exceptional secondary, (Fournier), 523 (Abst.)  
     in ectopic pregnancy, value of, re-  
     sults of immediate operation and, (Koster and Sheinfeld), 93  
 Squamous cell carcinoma of cervix, (Goldstine), 137  
 Sterility due to ovarian dysfunction, (Jeffcoate), 913 (Abst.)  
 Sterilization, antihormonal, of female animals, (Magistris), 914 (Abst.)  
 Stoeckel's Handbuch der Gynäkologie, 448 (Book review)  
 Stork joins the blue eagle, (Margaretten), 447 (Book review)

Surgery, gynecologic, use of dilaudid in, (Brown and Kleine), 89  
     in retrodisplacement of uterus, when in-  
     dicated, (Gardner), 596, 749  
     of abdominal and pelvic regions, (Ken-  
     nedy), 752 (Book review)  
 Surgical treatment of ovarian dysfunc-  
 tions, (Robinson), 18  
 Sutures, silver wire, prevention of exco-  
 riation of perineum from, (Grad), 863  
 Sympathectomy, presacral, treatment of  
 dysmenorrhea by, (Keene), 534, 740  
 Syphilis, hereditary, and cancer of cer-  
 vix, (Pauco), 303 (Abst.)  
 Symphysiotomy for after-coming head, (Falsia), 263 (Abst.)

T

Temperature, premenstrual elevation of, (v. Fekete), 385 (Abst.)  
 Test, sex prediction, of Dorn and Sugar-  
 man, (Pommerecke and Rogers), 380  
 Theca cell tumors, (Geist), 480, 901  
 Theelin and galactin, experiments with,  
     on growth and function of mam-  
     mary glands of monkey, (Allen,  
     Gardner, and Diddle), 912 (Abst.)  
 Therapie der Frauenkrankheiten, (Ben-  
 thin), 753 (Book review)  
 Thermo therapy, influence of local, upon  
     temperature of deep genital  
     sphere, (Nizza), 727 (Abst.)  
 Thorium preparations, intravenous injec-  
     tion of, histologic clunings in rab-  
     bits and in dogs following, (Shute  
     and Davis), 605 (Abst.)  
 Torsion of pregnant uterus in patients  
     with kyphotic pelvis, (Rabbiner),  
     136  
 Toxemia of late pregnancy, (Thomas,  
     Allen, Bauer, and Freeland), 665  
     of pregnancy, (Goodall), 577, 876;  
     (Oberst and Woods), 232  
 Transfusion, blood, in treatment of obstet-  
     ric hemorrhage, rôle of, (Dieck-  
     mann and Daily), 1  
 Trauma, artificial reduction of blood  
     pressure by, effects of injection of  
     50 per cent glucose solution before  
     and after, (Mazzola and Torrey),  
     339  
     birth, in cancer of uterine cervix, fac-  
     tor of, (Maefarlane), 133  
 Traumatic hemorrhage from vagina,  
     (Ghosh), 703 (Abst.)  
 Tribromethynol premedication in opera-  
     tive gynecology, (Reycraft), 332  
 Trichomonas vaginalis among Japanese  
     women, (Ohga and Aoji), 338  
     (Abst.)  
     clinical and bacteriologic observa-  
     tions in, (Allen, Jensen, and  
     Wood), 565, 736  
 Tubal gestation, (Tyronne, Romano, and  
     Collins), 112  
     reimplantation—in retrospect, (Tar-  
     nowsky), 696  
     twin pregnancy, full-term unilateral,  
     (Ferguson and Otis), 139  
 Tube, carcinoma of, (Vignes), 288 (Abst.)  
     for collection of urine under aseptic  
     conditions, (Litt), 433  
 Tuberculosis of cervix uteri, (Counsellor  
     and Collins), 830  
 Tuberculous adnexitis, radiotherapy of,  
     (Gilbert), 605 (Abst.)  
     endometritis, (Diehelm and Ramsey),  
     420  
 Tumor, Brenner, of ovary, (Smith), 734  
     corpus luteum, (Cutler), 131  
     Krukenberg, pathogenesis of, (Puhr),  
     589 (Abst.)  
     of female pelvic organs, (Meigs), 449  
     (Book review)



## Tumor—Cont'd

- of ovary, (Gery and Adrian), 674 (Abst.)
- ovarian, histogenesis of certain, and their biologic effects, (Geist), 650
- theca cell, (Gelst), 480, 901
- Twin, anencephalic, (Litt and Strauss), 728
- monoamniotic, one normal, the other anencephalic, (Litt and Strauss), 728
- pregnancy, fetus papyraceous in, (Crotty), 296
- full-term unilateral tubal, (Ferguson and Otis), 139
- value of finger prints in, (Bak), 709 (Abst.)
- Typhoid abscess, chronic, of ovary, (Soloff and Hermann), 290

## U

- Uleer, elusive, of bladder, treatment of, by application of pure phenol, (Sears), 85
- of stomach and cancer as complications of labor, (Grüné), 307 (Abst.)
- Unbilical hernia, congenital, operative treatment of, (Ludwig), 208 (Abst.)
- Unvermutet Schnelle Tod in Schwangerschaft, Eburn und Woehebett, (Kehrer), 444 (Book review)
- Urethra, female, cancer of, (Auer), 318
- melanoma of, (Rosenthal), 115
- Urinary tract during pregnancy, physiologic changes occurring in, (Hundley, Walton, Hibbitts, Siegel, and Braek), 625, 885
- Urine, pregnancy, results of preoperative administration of an extract of, (Hamblen), 913 (Abst.)
- tube for collection of, under aseptic conditions, (Litt), 433
- Uterine and vaginal prolapse, colpectomy in treatment of, place of, (Phaneuf), 544, 872
- cancer, statistics of, (Terada), 135 (Abst.)
- carcinoma, 152 (Abst.)
- cervix, cancer of, factor of birth trauma in, (Macfarlane), 133
- carcinoma of, histologic grading in, (Jorstad and Auer), 153 (Abst.)
- disease, benign, total versus subtotal abdominal hysterectomy in, (Richardson), 237
- epithelioma, gonadotropic hormone in, experimental researches on, (Cornell and Escarraz), 914 (Abst.)
- hemorrhage, (Witherspoon), 762 (Abst.)
- motility in unanesthetized rabbits, comparative actions of crystalline progestin and crude progestin on, (Allen and Reynolds), 309
- prolapse and carcinoma of portio, coincidence of, (Haegler), 153 (Abst.)
- cancer of cervix in cases of, (Tourneux), 152 (Abst.)
- Uterovarian atrophy with persistent lactation (Frommel's disease), historical review of syndrome embracing, (Sharp), 411
- Uterus, adenocarcinoma of fundus of, (Goldstine), 137
- and ovaries, malignant diseases of, experience with multiple dose roentgen therapy in, (Healy), 613, 904
- cancer of, in childhood, (Lockhart), 76

## Uterus—Cont'd

- double, pregnancy in patient with complete, (Green and Miller), 281
- infantile and deficient human, studies on, (Clauberg), 867, (Abst.)
- inversion of, in two successive pregnancies, (Fox), 295
- motility in transplanted, denervated, (Kaminester and Reynolds), 395
- pregnant, torsion of, in patients with kyphotic pelvis, (Rabbiner), 136
- retrodisplacement of, when is surgery indicated in, (Gardner), 596, 749
- retroversion of, (Luker), 300 (Abst.)
- sarcoma and adenocarcinoma of body of, (Goldstine), 143

## V

- Vagina, artificial, creation of an, vaginal aplasia and, (Israel), 273
- cancer of cervix and, in case of complete procidentia, (Brady), 277
- traumatic hemorrhage from, (Ghosh), 703 (Abst.)
- Vaginal and uterine prolapse, colpectomy in treatment of, place of, (Phaneuf), 544, 872
- antiseptics during labor, mereurochrome to secure, (Mayes), 80
- aplasia and creation of an artificial vagina, (Israel), 273
- hysterectomies performed for benign disease with three deaths, series of 627, (Heaney), 269
- insulin treatment of cervical erosions, theory and results of, (Klaften), 543 (Abst.)
- speculum, a modified, (Fullerton), 297
- Vaginitis, gonococcal, in children, experiences with amniotin in treatment of, (Telinde and Brawner), 512, 887
- pyridium in treatment of, in children, (Brown et al.), 198 (Abst.)
- trichomonas, clinical and bacteriologic observations in, (Allen, Jensen, and Wood), 565, 736
- Varicose veins, injection of, during pregnancy, (Cheatham and Peck), 392
- Vascular injection, accidental, in course of hysterosalpingography, (Béclère), 604 (Abst.)
- Veins, varicose, injection of, during pregnancy, (Cheatham and Peck), 392
- Veratrum viride in treatment of eclampsia, (Bryant), 46
- Vesicovaginal fistulas, treatment of, (Miller), 675

## W

- Washington Gynecological Society, transactions of, 908
- Weibliche Geschlechtsorgane und Unfall, (Mayer), 449 (Book review)
- Wertheim's operation, treatment of carcinoma of cervix by, (Bonney), 815
- Women, hypothyroidism as a problem in, (Davis), 570, 742

## X

- X-ray treatment of diseases of genitourinary system, (Orton), 840 (Abst.)
- pregnancy after, of mother, (Tesauero), 606 (Abst.)

## Z

- Zondek-Ashheim test after partial hypophysectomy, (Stern), 912 (Abst.)

